# Analysis and Synthesis in Nineteenth-Century Organic Chemistry

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Dissertation submitted in partial fulfilment of the

PhD degree of the University of London

December 2008

## Declaration

I, Catherine Mary Jackson, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

## Abstract

This dissertation examines the development of synthetic organic chemistry in academic laboratories in nineteenth-century Germany. By studying the laboratory practice of chemists including Justus Liebig, August Hofmann and Albert Ladenburg, I show that early *synthetical experiments* were undertaken with primarily analytical goals, and that construction did not become the dominant purpose of organic synthesis until around 1880. I argue that successful constructive synthesis depended on a new glassware based practice whose unprecedented scale and intrinsic danger drove the construction of purpose-built chemical laboratories from the 1860s onwards. I therefore propose both a revised historiography of nineteenth-century organic chemistry, and a reinterpretation of the *institutional revolution* in late-nineteenth century physical sciences.

I re-examine Liebig's motives for tackling the analysis of alkaloids, using his 1830 laboratory notebook to reconstruct Liebig's experimental approach to this technically demanding task, including his development of a new apparatus for the determination of carbon – the *Kaliapparat*. I show that incorporating analysis using the *Kaliapparat* into a reliable, pedagogically stable method involved the labour of the entire Giessen research school. Liebig, his students and assistants produced new chemical knowledge from indeterminate analytical data by a combination of theoretical and practical expertise acquired through disciplined laboratory training, and I argue that a similar *philosophy of practice* was equally essential in synthetic organic chemistry. Synthesis made chemical identity a focus of chemists' practical concern and I demonstrate that purity, transformation and identity were central to Hofmann's constitutional analysis and Ladenburg's eventual synthesis of the hemlock alkaloid coniine. I explore the origins of what I term the *glassware revolution*, and its role in resolving the question of chemical identity. Finally, I show how Ladenburg's synthesis depended on glass and glassblowing, and I argue that this new chemical practice both produced and depended on highly organised, specialised laboratory spaces.

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# Introduction

This is a history of synthetic organic chemistry, that part of organic chemistry concerned with the construction of compounds of the element carbon from simpler substances. This constructive power, frequently if erroneously credited with an early-nineteenth century rejection of vitalism, continues to encourage synthetic organic chemists' belief in the uniqueness of their discipline. "Chemistry creates its object," asserted the arch-propagandist for organic synthesis Marcellin Berthelot in 1876, and this grandeur of ambition has been central to what I would like to call the romantic view of synthetic organic chemistry ever since.[1] As the eminent synthetic chemist Robert Burns Woodward put it almost 100 years later, "The unique challenge which chemical synthesis provides for the creative imagination and the skilled hands ensures that it will endure as long as men write books, paint pictures, and fashion things which are beautiful, or practical, or both".[2] This romantic consciousness has found an outlet in numerous histories of organic synthesis, many of them dating from its early heyday and mainly written by retired practitioners of the discipline, yet we still lack any history which *explains* the origins and development of synthetic organic chemistry as an academic discipline during the nineteenth century.

The first book length history devoted to organic chemistry was Carl Schorlemmer's 1879 *The Rise and Development of Organic Chemistry*. Schorlemmer, the first Professor of Organic Chemistry at Owens College in Manchester, presented his readers with a progressive and celebratory account of the origins and achievements of organic chemistry in general, and synthesis in particular.[3] Some forty years later Carl Graebe's *History of Organic Chemistry* was able to look back with still greater pride on the many and various successes of late-nineteenth century organic synthesis, including Graebe's own role in the synthesis (with Carl Liebermann) of the natural dye alizarin and the epoch-making work of Emil Fischer in the synthesis and structural elucidation of sugars.[4] In both cases, synthesis was made to seem the ultimate and inevitable goal of organic chemistry, *for which no explanation was required*. In recent times, moreover, the history of organic synthesis has largely failed to attract the attention of professional historians of science.[5] Organic synthesis necessarily received some coverage in studies of closely related topics,

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[1] Berthelot 1876, 275.
[2] Woodward (1963, 21) as quoted in Brock (1992, 633).
[3] Schorlemmer 1879.
[4] Graebe 1972 [1920].
[5] Some exceptions to this are: Brooke 1971; Russell 1987; Russell 2004.

such as the history of stereochemistry, but the only recent book with synthetic organic chemistry as its explicit focus is the popular history *Chasing the Molecule* – which was also written by a retired chemist.[6]

The purpose of this dissertation is to provide a history which explains the origins and development of the academic discipline of synthetic organic chemistry during the nineteenth century. My study shows that synthetic organic chemistry emerged around 1840 in response to difficulties encountered within the analytical programme in Justus Liebig's Giessen laboratory. I argue that early *synthetical experiments*, pioneered by Liebig's pupils including August Hofmann, were performed in pursuit of primarily analytical goals, playing an especially important role in the vexed question of assigning chemical identity. Contrary to accepted historiography, I propose that construction was not initially the dominant purpose of synthetic organic chemistry, only becoming so during the latter decades of the nineteenth century in the hands of a third generation of chemists.

Synthetical experiments produced a vast body of accumulated chemical knowledge concerning the constitution and reactivity of numerous classes of organic substance, and they provided the foundations upon which *synthetic organic chemists*, exemplified in this study by Albert Ladenburg, were able to build constructive synthesis. Converting the somewhat general understanding of chemical transformations produced by synthetical experiments into highly specific reactions required for the construction of particular molecular targets was, however, no simple matter. Whether in purification, identification or the performance of a chemical reaction, constructive synthesis demanded new levels of precision and control, which chemists like Ladenburg achieved through unprecedented dependence on glass apparatus and glassblowing. I argue that these novel uses of glassware are a highly significant defining feature of the new practice of constructive synthesis which, in its turn, marks an important historical discontinuity. Synthesis, moreover, produced many new substances, whose unknown properties dramatically increased existing laboratory hazards due to fire and explosion, and to chemists' exposure to harmful substances. Especially in the context of large-scale pedagogy, I argue that the effective management of such risks was significant in driving and shaping the construction of purpose-built institutional chemical laboratories during the second-half of the nineteenth century, and I show how this view leads to a revision of what is usually known as the *laboratory revolution* in chemistry.

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[6] Travis 1993; Ramberg 2003; c.f. Buckingham 2004.

In this introductory chapter I set out the strategies I have used to achieve these major historiographical revisions. The chemists' histories I referred to above are united in attributing the development of organic synthesis to Liebig, a view which – because those expert, contemporary sources have been regarded as largely beyond historical analysis – has persisted in modern historical writing about Liebig. We derive our view of Liebig and his students as a research school from Jack Morrell's comparative study of Thomas Thomson in Glasgow and Justus Liebig in Giessen, Liebig having provided Morrell with his model successful research school.[7] Yet, as I discuss below, Morrell – though he emphasised the importance of treating training and research as an integrated whole – did not pursue the implications of this approach for Liebig's role as the originator of organic synthesis.[8] And although Morrell's essay prompted numerous more detailed studies of Liebig and his laboratory, this literature has tended to follow Morrell in accepting the standard view of the development of synthesis whilst at the same time abandoning the potentially powerful tool for its deconstruction provided by training-research integration.

Treating research and training as an integrated whole, on the other hand, opens up new historical approaches – developed and applied largely in the history of physics – which emphasise precisely those links between pedagogy and practice that remain missing from the history of organic chemistry. By focusing on the daily laboratory *practice* of organic chemists, therefore, the current work emphasises aspects of the history of nineteenth-century organic chemistry which are overlooked in existing histories, whether they are predominantly concerned with theory or training. The study of practice, for example, exposes and illuminates the intimate relationship between theory and experiment which, I want to make clear from the outset, is one of the central points for discussion in this dissertation.

The nature and scope of this study have affected the sources I have used, and the ways in which I have used them. Although central parts of my argument are built on the study of archival material, I have used mainly primary published material elsewhere. I make no apology for this; indeed I argue that – in searching for the major landmarks of *disciplinary* development – published, communal discourse is a far more reliable and relevant initial guide than the essentially private world of the personal archive. Much writing in the history of science tacitly assumes that greater archival detail necessarily produces more authentic history but I suggest that, whilst archives certainly display individual idiosyncrasy in a way that other sources cannot,

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[7] Morrell 1972.
[8] Ibid., 8.

journal articles and other communally published materials better reflect accepted disciplinary thinking. The recent availability of online journals has, furthermore, enabled new research methods without which it would not have been possible to write a dissertation of such breadth. The ability to search electronically whole runs of journals for particular terms and phrases allows extraordinarily rapid access to material previously only to be found by the painstaking and time-consuming process of paging through every volume in hard copy. Though I have used them throughout, these tools were essential in my studies of synthesis and glassware. In the final section of this *Introduction* I set out an overview of the chapters which follow, emphasising their most significant claims to originality.

## Research Schools and the History of Nineteenth-Century Organic Chemistry

Notwithstanding historians' neglect of synthetic chemistry, nineteenth-century organic chemistry remains one of the most-studied parts of the history of chemistry as a whole. Biographies of famous chemists including Justus Liebig, who plays a major role in the current study, are partly responsible for this but Morrell's research school essay was also a major impetus to work in this area.[9] The rapidly professionalizing discipline of nineteenth-century chemistry provided particularly rich material for Morrell's approach, and his work struck a chord with prevailing themes within the discipline of history of science in the early 1970s because it provided a tool with which historians were able to integrate social, cultural and technical aspects of their field of study. As a result, Morrell's work was exceptionally effective in drawing history of chemistry to the attention of late-twentieth century historians of science.[10]

Morrell's research school proved to be "an uncommonly fruitful unit of analysis" according to Gerald Geison, whose monograph study of Michael Foster's physiological laboratory was one of many to apply the concept outside its original disciplinary context.[11] Its wide applicability, however, did not diminish the appeal of the research school to historians of chemistry, and the 1993 collection of essays edited by Geison with Frederic Holmes included a number of valuable contributions to the history of nineteenth-century chemistry. Mary Jo Nye's discussion of national

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[9] Brock 1997; Morrell 1972. For a recent review of the research school concept in the history of chemistry, see Jackson 2006.
[10] The professionalization of chemistry has been widely discussed. Homburg (1998 and 1999) are especially relevant for the German case. On Britain, see Bud and Roberts 1984.
[11] Geison 1993, 228. Geison (1978) was the first book length study of a research school.

styles of nineteenth-century chemistry focused on the differences between France and Britain, whilst Alan Rocke compared Hermann Kolbe's research groups at Marburg and Leipzig. Morrell's own essay in that volume was candid about the limitations of the research school as originally introduced, but Morrell persisted in emphasizing its value and significance as a unifying influence within the history of science, and more generally between history of science and wider cultural history.[12]

One especially important aspect of that unifying influence was Morrell's commitment to the intimate connection between training and research, a relationship which was also central to the notion of "normal science" spelt out some ten years earlier by Thomas Kuhn.[13] Morrell envisaged Liebig's laboratory as a "knowledge factory ... characterized by the steady and systematic production of reliable experimental results by ordinary students whose scientific mediocrity had been converted into scientific competence" by training. The success of this enterprise depended, amongst other things, on "relatively simple, fast and reliable experimental techniques" which were "applied to a body of related problems", ideally in a field without strong competition.[14] Training in Giessen included qualitative and quantitative analysis,[15] as well as the preparation of pure substances from raw materials, and it equipped students to participate in Liebig's largely experimentally based research programme to determine the composition and investigate the chemical transformations of organic compounds derived from natural sources. Liebig's choice to study this "relatively unexplored new branch of chemistry" through the application of his recent, simpler method for quantitative organic analysis was, Morrell argued, significant in enabling the routine training of students for large-scale research.[16]

In addition to its influence on history of chemistry and history of science more generally, Morrell's essay prompted a number of important studies of Liebig's laboratory, most notably those of Joseph Fruton and Frederic Holmes.[17] Their work

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[12] Geison and Holmes 1993, in which Nye 1993, Rocke 1993a, and Morrell 1993 appear.
[13] Kuhn 1996 [1962], later emphasized in Kuhn 1977, Chapter 9. For a recent analysis of the role of pedagogy in "normal science", see Warwick and Kaiser 2005.
[14] Morrell 1972, 5.
[15] Qualitative analysis of an inorganic substance in order to determine which elements it contains was the first stage of practical chemical training in the early nineteenth century. Organic substances, which usually contain only carbon, hydrogen, oxygen and (sometimes) nitrogen, were examined by accurate quantitative analysis to measure their composition, i.e. the percentage by mass of these constituent elements. This technique was taught on a large scale for the first time in Giessen, where it formed the basis of advanced practical training in Liebig's laboratory school.
[16] Morrell 1972, 8, 10.
[17] Fruton 1988; Holmes 1989a.

disputed many of Morrell's specific claims about Liebig's approach to training, in some instances leading to on-going debates in the history of chemistry. Holmes, for example, viewed the system of training in Giessen as a response to contemporary disciplinary trends rather than a product of Liebig's chemical intuition. Others including Ernst Homburg questioned the extent to which Liebig's progressive system of instruction was innovative, arguing that it was merely a new application of methods developed in earlier pharmaceutical training schools, particularly that of Friedrich Strohmeyer – claims which have been convincingly refuted by Rocke.[18] Because of its emphasis on training, however, most of this writing about Liebig's laboratory has also – like research school literature in general – tended to treat teaching and research as separate activities, thereby rejecting or at least side-stepping one of Morrell's key modes of integration. One consequence of this response is that absolutely central questions concerning the relationship between training and research in Giessen have yet to be addressed. We have, for example, no detailed understanding of how Liebig was able to transform the experimental work of relatively inexperienced chemists into useful research, nor of exactly what kind of training young chemists received in Giessen, nor of how – in the case of those who went on to pursue chemical research – such training affected their future investigative and experimental practice.

These questions have a bearing on two significant issues: one within the history of nineteenth-century chemistry, but the other relevant to the history of science more broadly. The specific issue is this: the history of nineteenth-century chemistry is dominated by the rise of large-scale laboratory training on the one hand and the growth of the synthetic dye industry on the other, with Liebig generally given credit as the originator of both. Yet we have no account *at all* of how the Giessen system of training, centred on techniques of quantitative organic *analysis*, could lead to the development of *synthetic* organic chemistry within either academic or industrial contexts. The lack of any such explanatory account reflects the general neglect of synthetic organic chemistry in the existing historical literature. Historians of chemistry have simply not asked such questions, mainly because they regard the development of organic synthesis as requiring no explanation but also because, as I mentioned earlier, interest in synthesis has tended to arise only insofar as it touches on other historical and philosophical questions. Not only has organic synthesis been seen as inevitable but it also did not offer much for historians of ideas to get their

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[18] See Homburg (1999) on Friedrich Strohmeyer's earlier teaching laboratory in Göttingen; and the response in Rocke 2003.

teeth into, with the result that we have histories of industrial synthesis in the late-nineteenth and early-twentieth centuries and numerous accounts – many of them historically misleading – of the impact of organic synthesis on belief in a vital force, but no history which explains the origins and development of synthetic organic chemistry as an academic discipline during the mid-nineteenth century.[19]

In more general terms, re-examining Liebig's research school in order to discover the intricate interplay between training and research in Giessen, and how such training prompted chemists to introduce synthesis alongside analysis in their repertoire of investigative skills, speaks to important developments in our understanding of the links between pedagogy and practice which have emerged from other areas of the history of science. Kathryn Olesko's detailed study of Franz Neumann's Königsberg physics seminar described the methods by which Neumann systematically introduced his students to the tools of research. Olesko did *not* characterise Neumann's seminar as a research school because it lacked a shared family of problems, but her work nevertheless showed that Neumann faced many difficulties common to the directors of research schools. Although Neumann originally envisaged teaching "as a vehicle for extending mathematical methods into new areas in physics", for example, he was forced to modify his plans to accommodate his students' generally rather limited mathematical abilities. As a result, the Königsberg seminar became based on quantitative methods, including errors and instrumentation, which were relatively minor themes in Neumann's own, more mathematical research.[20]

More recently, Andrew Warwick's study of mathematical physics in mid-Victorian Cambridge provided a detailed model for how routine skills – in this case mathematical problem solving using the differential calculus – can be translated into research.[21] Warwick showed that pedagogy is a vital component in the creation of a local research community with a shared understanding of which problems are important and what would constitute their acceptable solution, and he used the case of the British reception of the special theory of relativity to demonstrate the difficulty of transferring new knowledge between such communities.[22] Warwick also, and

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[19] Ramberg (2000) has shown that many textbooks of organic chemistry assign a decisive role in the death of vitalism to Wöhler's preparation of urea. Brooke (1968), meanwhile, explored the significance of this preparation in primarily philosophical rather than historical terms.

[20] Olesko 1991a, 8-11.

[21] See Warwick (2003, Chapter 6) on the emergence of the Maxwellian research school of electromagnetic theory.

[22] See, in particular, Warwick's (2003) conclusion to Chapter 8.

unlike previous work in this area, made explicit the revolutionary nature and productive power of nineteenth-century pedagogical techniques involving the minute management of time, space and the self.[23] The Cambridge Wrangler-making system emphasized disciplined living, including long hours of intense study aimed initially at mastering exemplar solutions.[24] It also depended crucially on the "subtle manipulation of student sensibilities that seemed only to occur in the intimate atmosphere of the coaching room", where "students picked up part of the coach's unique approach to mathematics, an approach which could not be learned simply from the unsupervised use of textbooks and private study".[25]

I have shown elsewhere that there are many parallels between the training of chemists in Giessen and the system of mathematical training described by Warwick, but that there are also important differences between the two forms of scientific practice.[26] As William Brock noted, Giessen chemists – like would-be Wranglers – followed a rigorous training in solving standard, graded problems during which they were subjected to regular examination.[27] Both systems of training demanded long hours of hard work from even the most talented students and necessitated abstinence from traditional student dissipations and amusements. But whereas the intellectual intensity of the mathematical physicist's solitary work was often counterbalanced by the vigorous physical exertion of running or rowing, the communal laboratory setting and collective nature of chemists' labour involved their physical selves in a quite different way. Doing chemistry made demands on the body as well as the mind, and it brought the student into immediate contact with the material world in a way that mathematics did not. "Chemistry", as Michael Faraday explained in 1827, "is necessarily an experimental science" and every experiment, once devised, has to be *performed*. I do not agree with, and will present considerable evidence in this dissertation to refute, Faraday's assertion that organic analysis is "essentially dependent for success on *mere* manipulation" but his emphasis on the importance of the chemist's manipulative skill certainly reminds us

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[23] Warwick (2003, Chapter 1) and references therein to Foucault 1977. Joseph Rouse (1987) also recognized the very close links between Foucault's ideas and those of Jerome Ravetz (1971) and Bruno Latour (1987).
[24] Wrangler was the name for those who gained a first class degree in the Cambridge Mathematical Tripos.
[25] See Warwick (2003, Chapter 4) on the discipline demanded of students by the Cambridge Mathematical Tripos; and Chapter 5 on the coaching system that arose to support the rigours of such competitive training. The direct quotations are from pp. 241 and 228 respectively.
[26] Jackson 2006.
[27] Brock 1997, 45-6.

that the history of chemistry is woefully incomplete without a history of chemical practice.[28]

## The Practice of Analysis and Synthesis in Organic Chemistry

It is, furthermore, *essential* for writing this history of the development of synthetic organic chemistry that I have studied the practices of nineteenth-century chemists. I mentioned earlier that organic synthesis has been almost entirely overlooked by historians of ideas, and the same might well be said of organic analysis and for exactly the same reasons. In both cases, chemists' investigative goals have frequently been considered by historians to have little to do with chemical theory, synthesis involving the (implicitly straightforward) construction of substances of known composition and structure whilst analysis was a routine manipulation whose results enabled chemists to discover composition and formula by simple deduction from experimental data. Viewed from the perspective of theory development, both analysis and synthesis become virtually invisible, effectively effaced from the history of organic chemistry.

This phenomenon, which I should like to call *theoretical transparency*, occurs wherever emphasis on theoretical innovation blinds historians to the everyday labour involved in doing science, and it can be associated with theoretical as well as practical activity. In the case of mathematical physics, for example, Warwick used "paper, ink and wickerwork" to expose a previously unnoticed practice of theory in one of the most-studied disciplines in the history of science.[29] The study of practice focuses historical attention on the scale and nature of the work involved in performing tasks which appear at first sight to have little connection to theory. One consequence of this is that studying practice has the potential to bring to light previously unsuspected connections between practice and theory. As Ursula Klein has shown, the practice of nineteenth-century organic chemistry, particularly organic analysis, included powerful theoretical manipulations in which formulae functioned as "paper tools".[30] It also, as this dissertation will argue, supports a model of the relationship between scientific theory and practice in which practice, far from being subservient to theory, is essentially constitutive of it. By examining the laboratory practice of nineteenth-century chemists, I show that – however great their interest in contemporary theoretical questions – the majority of their working life was spent

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[28] Faraday 1827, i-iii. Emphasis added.
[29] Warwick 2003, 17.
[30] Klein 2003.

extracting, purifying, crystallising; analysing and reacting; blowing glass and measuring melting points. This immense labour, moreover, was an essential component of the environment in which chemical theory could be created and put to work. Not only is organic synthesis worthy of historical attention, I claim, but it is hard to see how to write the history of nineteenth-century chemistry without it.

Discovering and understanding what chemists were *doing* in the nineteenth century helps us to see the nature and extent of the difficulties they faced, and makes visible the strategies they adopted in attempting to overcome those obstacles. By finding out what chemists like Liebig and his pupil August Hofmann hoped to achieve, moreover, we learn that both organic analysis and synthesis depended on the integration of theory and experiment, and that organic synthesis in particular was very far from being theoretically insignificant. On the contrary, we see for the first time *why* chemists like Hofmann began to make the move from analysis to synthesis during the 1840s, and how synthesis itself developed side-by-side with chemical theories, changing its meaning and purpose in the process. Early *synthetical experiments* were intended to elucidate the arrangement of elements within organic substances, and their results were incorporated into hotly debated theories of constitution.[31] The accumulation of a vast body of such experimental data eventually contributed to the resolution of those debates, and it enabled chemists to attempt the construction of organic substances, but the one did not cause the other. On the contrary, and as I argue in this thesis, constructive syntheses were both attempted *and achieved* well before the establishment of structural theory, or any notion of the position of atoms in three-dimensional space.

That it should have taken so long for the history of chemistry to benefit from the insights afforded by the study of science as practice is, at first sight, somewhat surprising.[32] "There is no more eminently practical science than chemistry", pronounced the Scottish chemical educator David Reid in 1833, nobody being more aware of this disciplinary characteristic than the chemist himself.[33] So how is it that the history of chemistry, much of it written by chemists, has become primarily a history of theory?

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[31] The term "synthetical experiments" was first used in the context of organic chemistry by Muspratt and Hofmann 1843b, 367.
[32] Latour and Woolgar (1979) and Latour (1987) are the key anthropological studies which sparked investigation of science as practice.
[33] Reid 1833.

## Theory and Practice Reunited

I think there are two related causes. First, histories of chemistry since the nineteenth century have sought to promote the theoretical sophistication of chemistry in order to demonstrate its equality to or even superiority over mathematics and physics. Not only could the study of chemistry form the basis of a better liberal education than mathematics, chemists claimed, but the discovery of chemistry's laws promised a control over Nature whose human and economic benefits far exceeded anything likely to result from the study of physics.[34] Such histories, then, set a precedent for making chemistry resemble a branch of (preferably theoretical) physics which twentieth-century historians and philosophers of science, including many originally trained as physicists, were only too pleased to follow. Second, even where scholars have chosen to incorporate ideas of science as practice into their approach, they have done so predominantly in the area of physics. There is, for example, a small but highly significant body of literature concerned with nineteenth-century physics laboratories and the laboratory revolution, notably in the work of David Cahan on the rise of physics institutes in Imperial Germany and of Graeme Gooday on British laboratories including the Cavendish, whilst relatively little has been written about the design, construction, and operation of chemical laboratories in the same period.[35]

Not only is the study of practice a necessary, though hitherto largely neglected, approach to the history of chemistry, but I want to emphasise that the integration of theory and experiment was *essential* to the practice of both organic analysis and synthesis. Somewhat in the same vein as the notion of theoretical transparency discussed above is the idea that, whatever its previous state, organic analysis after Liebig depended on "*mere* manipulation" to obtain experimental results from which formulae could be deduced in a straightforward way. This view of organic analysis remains remarkably persistent in all but the most specialised, scholarly literature – even though it has been seriously undermined by recent work in the history of nineteenth-century organic chemistry. I have already mentioned Klein's exposure of the importance of chemical theory in making rational formulae (which included the chemist's understanding of a substance's constitution as well as its composition),

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[34] Liebig 1838b and 1840a; Baeyer 1878.
[35] Cahan 1985 and 1989; Gooday 1990. James (1989) is exemplary of the relative neglect of chemical laboratories. This collection of thirteen essays about the development of laboratory science in the nineteenth century contains only three essays about chemical laboratories, of which only two are concerned with the laboratory as a physical space.

and the productive power of those formulae in chemical thinking.[36] In addition, reconstructions of Liebig's experimental methods of analysis have enabled Melvyn Usselman, most recently together with Alan Rocke, to demonstrate that even composition was not simply determined by the results of analysis.[37] Together, these studies provide a valuable though still partial view of how chemical composition and constitution were actually produced from raw analytical data during the 1830s and 40s. They also suggest that the experimental practice of organic analysis was necessarily bound up *throughout* with other kinds of chemical knowledge. The present work pursues this theme, arguing that successful analysis according to Liebig's methods was incorporated within an extended *philosophy of practice* in which experimental skill as well as theoretical convictions guided the analyst along a highly uncertain path from experiment to formula.

Managing uncertainty was, of course, not confined to organic analysis and another of the main claims of this thesis is that such a philosophy of practice remained central to the investigative success of Liebig's pupils, most notably Hofmann, as they made the transition from analytical to synthetic organic chemistry. This continuity of practice is important in explaining how a Giessen training in analysis could equip chemists like Hofmann to enter the arena of synthetic chemistry, but it is also significant because it fundamentally challenges a widely held philosophical view of the relationship between analysis and synthesis in nineteenth-century chemistry. That view, brought to prominence in the polemical writings of Berthelot during the 1860s and 70s, cast analysis and synthesis as utterly distinct processes with entirely opposite goals: one destructive, the other constructive.[38] The current work, by contrast, shows that analysis and synthesis in organic chemistry were seen as complementary experimental approaches during the mid-nineteenth century, based on a shared philosophy of practice and directed towards the solution of key questions in common concerning chemical identity, behaviour and transformation. Such an understanding, moreover, brings organic chemistry into line with the current perception that combined analytical and synthetic techniques, together with reversible chemical processes, had been of great importance in the practice of *inorganic* chemistry since the eighteenth century.[39]

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[36] Klein 2003.
[37] Usselman 2003; Usselman et. al. 2005.
[38] Berthelot 1860, xi.
[39] See Klein and Lefèvre (2007, 115-116) on analysis and synthesis as complementary components of the analytical method; and p. 230 on the importance of reversible chemical transformations.

Restoring this continuity of practice between analytical and synthetic chemistry requires a new historiography for organic chemistry in the nineteenth century. If the original transition from analysis to synthesis did not re-direct chemical research towards the artificial construction of organic substances, then when, why and how did that change of purpose – which undoubtedly happened at some time during the nineteenth century – take place? I shall argue that construction, particularly of naturally occurring substances, did not become the dominant purpose of organic synthesis until around 1880. This development was certainly linked to chemists' increased constitutional and structural knowledge, but the relationship between synthesis and theories of constitution and structure was vastly more circular and more labour-intensive than usually recognised. Successful synthesis of a particular target compound was used to confirm ideas about its constitution, but synthesis also provided the most significant body of experimental data by means of which chemists were able to develop their more general constitutional and structural theories.

The new constructive chemistry presented challenges that could not be overcome by the existing practice of *synthetical experiments*. Achieving the preparation of a particular synthetic target by refining the outcome of specific chemical reactions until they produced the desired compound was a quite different matter from applying a series of well-studied transformations to a substance and identifying the products, whatever they might be. A new generation of *synthetic organic chemists*, exemplified in my study by the relatively little known Albert Ladenburg, developed a novel chemical practice based on new skills, many of which were unknown to their predecessors, however eminent. Seen from the perspective of practice, therefore, the emergence of synthetic organic chemistry as an independent sub-discipline no longer appears co-extensive with the history of great nineteenth-century chemists. Instead, individual chemists including Liebig and Hofmann are shown to have exerted greatest influence through their impact on the chemical community. This agency partly took the form of teaching, but it also involved setting an agreed, public agenda for the goals of research. Both Liebig and Hofmann, for example, promoted the artificial preparation of naturally occurring organic substances as an important goal for their discipline, and this shared disciplinary objective was important in directing the efforts of chemists like Ladenburg even though he had no immediate connection, pedagogical or otherwise, to either man.

What are the hallmarks of the alteration in chemical practice accompanying this shift in the goals of synthesis? A partial but nonetheless crucial answer to this question is: glass. It is, of course, such a commonplace that chemists' use of glassware

increased dramatically during the nineteenth century that this phenomenon has never seemed to require explanation.[40] I argue in this thesis that chemists' appropriation of glassblowing skill during the early decades of the nineteenth century led to far-reaching changes in chemical practice. In examining what I have called the *glassware revolution*, I show that skill in glassblowing enabled chemists to implement new ideas quickly, economically and without the mediation of specialist instrument makers. Some benefits of working in glass – its transparency and its inertia to a wide range of chemical substances, for example – had long been recognised, but others were new, or at least newly applied in chemical practice. Techniques of glassblowing made it relatively easy to create novel items of glassware for highly specific purposes with the result that the chemist-glassblower was able to respond swiftly to experimental outcomes, acquiring a new degree of flexibility and control over experimental spaces in the process. In particular, I show how the search for more sensitive methods of separation and more reliable methods of identification, as well as for increased specificity in processes of chemical transformation, drove chemists to innovate in glass.

## The Chemistry Set and the Laboratory

Basic glassblowing was incorporated into chemical training and, from at least the mid-century onwards, every chemist in Germany could be expected to know something of the glassblower's craft. I contend that their use of glassware was essential to organic chemists' development of constructive synthesis, making it possible for them to obtain starting materials of previously unattainable purity which they then transformed by means of increasingly specific reactions into the desired chemical target. At the same time, I show that the production of particularly complex pieces of glassware and the standardisation of new items of apparatus for manufacture usually continued to involve collaboration between chemists and highly skilled glassblowers. By the late-nineteenth century, both custom-made glassware and novel assemblies of manufactured components were used in the minute management of pressure and temperature, mixing and separation, giving chemists access to an unprecedented variety of finely tuned experimental methods which were applied to the construction of a wide variety of natural and artificial organic substances.

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[40] See, for example, Russell 2002.

These uses of glassware made possible the development of organic synthesis, but the presence of this new chemistry set on every chemist's bench also made unprecedented demands on the laboratory environment. Glass vessels containing reactive and frequently toxic chemicals, often maintained at high temperature and extreme pressure, proved quite literally explosive. The production of previously unknown substances by synthesis, moreover, was accompanied by increased uncertainty regarding their chemical and physiological properties. Doing chemistry is well known to be dangerous, but I argue that practice of synthetic organic chemistry in glass – particularly in the context of large-scale laboratory training – marks a watershed in the history of this danger. Not only were synthetic organic chemists exposed to the immediate risks of explosion and acute poisoning but many new substances also posed long-term risks including the potential to cause chronic, sometimes terminal, illnesses. In the hands of an expert practitioner working alone, such risks might usually be manageable by individual experience and responsibility. In the context of large-scale teaching, however, they had profound implications for both the structure and discipline of training and for the physical space of the laboratory, and I argue that managing risk and pedagogy played a decisive role in the design and construction of purpose-built chemical laboratories during the nineteenth century. This idea is not entirely new, but it has so far only been recognised in very specific contexts. We already know, for example, that Liebig's newly extended laboratory in Giessen included primitive enclosures intended to reduce the concentration of fumes in the atmosphere, but otherwise very little attention has been paid to the effect of chemical practice – particularly of a large number of trainee chemists in a confined space – on the desirable layout and organisation of the laboratory.[41]

To the limited extent that historians have studied the construction of large-scale institutional chemical laboratories in the second-half of the nineteenth century, moreover, they have done so with exclusively social historical questions in mind.[42] As a result, there is nothing in the history of chemical laboratories comparable to Simon Schaffer's exposition of the metrological influence exerted by the Cavendish Laboratory, with its useful lessons about the motives and arguments for introducing laboratory training in physics, and the kinds of physical spaces and allied resources that were required for the successful establishment and propagation of that

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[41] Brock 1997, 58; and Appendix 1, pp. 333-341.
[42] See, for example, Borscheid 1976 and Tuchman 1993.

training.[43] This omission is all the more surprising given the existence of numerous published, contemporary accounts in which chemists themselves addressed exactly these questions, and I have made extensive use of these sources to show how laboratory design changed in response to chemical training and research. Chemistry's economic significance in agriculture, medicine and manufacture was essential in funding the building of new chemical laboratories, but I will show how the day-to-day practice of chemists at the bench prompted, drove and shaped what is usually thought of today as the *laboratory revolution* in chemistry.

## Sources

Given the extent of my repeated references to Liebig and, to a lesser degree, to his pupil Hofmann, I think it is worth emphasising that this is neither a biographical study, nor a prosopography. This history of organic synthesis concentrates on the work of three chemists spanning three generations: Liebig, Hofmann and Ladenburg, but its scope is both wider and more limited than this suggests. I have made no attempt at an exhaustive discussion of the work of any of these men, let alone their entire life stories, even though Liebig is the only one of the three for whom a modern biography exists. Biographical studies of Hofmann and Ladenburg would be valuable additions to the history of nineteenth-century chemistry, were adequate source material to be available to support such work, but that has not been my goal here. My story also mentions a large number of other people and institutions, several of them already subjected to the historian's gaze but many of them virtually unknown; all of them are ripe for further investigation. Indeed, this thesis makes no claim to be the final word on any point of detail. Instead, it sets out a new, broad and causal history of the transition from analytical to synthetic chemistry which I hope will be of interest to both historians of science and practising chemists.

The breadth of scope and the aims of this thesis have had a direct bearing on the kinds of sources I have used. Perhaps somewhat unusually for a work of scholarly history of science written early in the twenty-first century, this is not based in the first instance on an exposition of the contents of previously unstudied archival material. To some extent this is an inevitable consequence of the nature of the subject matter, but it also reflects a positive choice on my part. With the exception of Ladenburg, the chemists who feature most in this dissertation were prominent figures whose

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[43] Gooday 1990; Schaffer 1992. Where historians have addressed chemistry laboratories, they have generally concentrated on the period up to and including the eighteenth century. See, for example, Holmes 1989b and Crosland's (2005) discussion of laboratories as the location of experimental science.

lives and work have been subjected to considerable previous historical scrutiny but, as my study of Liebig's 1830 notebook illustrates, there is still plenty of scope for further archival work.[44] The use of published material offered a number of important advantages in a project of this kind. For one thing, it made it possible for this dissertation to cover a considerably more extended geographical and temporal range than would have been achievable using archive materials, particularly in a second language. In the case of published papers, moreover, the ability to search online collections enabled forms of research which were previously impracticable. With these new tools, for example, following a particular topic through several journals over a period of decades is transformed from an extremely time-consuming process, likely to be a major component of any project, into a minor task whose output can be incorporated into a work of much larger scope.

I nevertheless want to emphasize that the reliance of this thesis on published material is by no means a second-best solution to purely practical limitations of time, patience and linguistic ability. This is, as I have explained, a history of the development of a chemical discipline, its pedagogy and practices, its material culture and its institutions. It is, in other words, a history of communal scientific activity and not of individual scientists. I therefore argue that published work has a relevance and importance in this context which the essentially private world of a personal archive cannot match. A personal diary may, for example, tell us a lot about its author's private reflections, and this may illuminate our view of that individual's attitudes and behaviour. If, as is the case here, our primary interest is in the disciplinary community to which the same person belonged, then the study of published work reflecting public, communal discourse ought surely to precede the excavation of such details from the archive. A careful and reflective reading of the available published material is, I think, a necessary precursor to drawing an accurate historiographical map of the subject without which it is futile, if not actively counter-productive, to delve into the archive.[45] Historiographical landmarks provide an essential overview of the scope, scale and dynamics of the historical landscape, archival material only acquiring its meaning in relation to this framework. If the landmarks are poorly chosen, then the resulting history will necessarily be flawed.

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[44] Brock (1981) examined the available sources on Liebig's life and work.
[45] Throughout this dissertation I have used the term historiography to refer to the landscape of and the important landmarks in history as defined by a particular historical approach.

## Overview

This introduction has laid out the broad strokes of a new history of nineteenth-century organic chemistry whose detail is filled in by the following chapters. My story opens in a small, provincial university town in the German state of Hessen in 1825 where a young chemist, who has until recently enjoyed the opportunities and excitement of scientific Paris, arrives to take up his first job. It is not the position he hoped for, but the young man's options were limited: he needed the money. Indeed, he was very lacking in experience and not particularly well qualified for this appointment, which did not go down too well with some of his new colleagues. In fact, the young man was something of a fish out of water socially, and he had no close family or friends nearby to support him.[46] Were it not for the benefit of historical hindsight, we would say this sounded like a difficult situation, one likely to test the young man's abilities, and certainly without any guarantee of a successful outcome. But of course we know exactly how this story ended. The young man in question Justus Liebig became the most famous chemist of the nineteenth century, drawing aspiring young chemists to his Giessen laboratory from all over the world and beginning a transformation by which German chemistry came to dominate the world for over half a century.

Knowing the ending has, to a greater or lesser degree, coloured every history we have of Liebig's life and work, including accounts of the foundation and expansion of his Giessen school and the establishment of his new method of quantitative organic analysis. Chapter One shows how different that story looks when we try to see things through Liebig's eyes, experience his isolation and uncertainty, and witness his struggle for recognition and influence both individually and through the work of students in his Giessen school. From the late 1820s until at least 1834, Liebig subjected himself to a punishing regime of work, driving himself to extremes of fatigue and instability. Viewed from this perspective, nothing about Liebig's phenomenal rise to fame seems preordained. On the contrary, his letters suggest that Liebig was often discouraged and disillusioned, even toying with the idea of giving up chemistry altogether. I argue that only overwhelming ambition, particularly to maintain and enhance his standing within Parisian scientific circles, and the support and encouragement of other chemists kept Liebig going during those periods where his work seemed unproductive and likely to go unrecognised and unrewarded.

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[46] This characterisation of the young Liebig is based on Brock's (1997) biography.

Liebig was certainly isolated when he first arrived in Giessen but I show that he nevertheless perceived himself to be part of a chemical *community*. Whether sparring with his Parisian rival Jean Baptiste Dumas, seeking consolation from his father figure Jöns Jacob Berzelius, or letting off steam in letters to his friend Friedrich Wöhler, Liebig's behaviour was that of a profoundly social being. Of course the desirability of considering even great men like Liebig within their social setting is by now widely accepted by historians of science, so what matters here is how this affects our understanding of Liebig's early professional life. For one thing, as my previous characterisation of his interaction with other chemists indicates, it prompts a significant re-appraisal of Liebig's social and scientific network. Not only do his relationships with Berzelius and Wöhler assume greater importance in stabilising Liebig's erratic and frequently fragile emotional state, but rivalry with Dumas emerges as a powerful influence on the direction of Liebig's early research. This view, moreover, suggests important new motives for the foundation and development of Liebig's Giessen research school. If chemical research was essentially a communal activity, what could be more rational for the isolated Liebig than to create his own community? And what could be more effective than shortage of material and financial resources in provoking him to build that community on a new economy of work and a novel experimental practice?

By the late 1820s, Liebig's research began to focus on the quantitative analysis of organic substances, including the family of nitrogenous organic bases now known as alkaloids, and in Chapter Two I examine Liebig's approach to this challenging investigative goal. Whilst performing an extensive series of alkaloid analyses in the autumn of 1830, Liebig introduced a new piece of glass apparatus for measuring their carbon content, later called the *Kaliapparat*. But although the *Kaliapparat* has frequently been credited with reducing the practice of quantitative organic analysis to a simple manipulative skill, this was certainly not the case for the analysis of alkaloids, the determination of whose composition remained highly problematic throughout the 1830s and 1840s. As my analysis of Liebig's 1830 laboratory notebook shows, neither the determination of carbon using the *Kaliapparat* nor the determination of nitrogen by any of the methods then available produced results which unambiguously determined either the composition or the formula of the alkaloid morphine. Instead, the raw results of analysis had to be considered within a much broader context including both additional experimental data and theories of chemical constitution and reactivity.

Even in the case of analytically less demanding substances, such as those containing no nitrogen, the conversion of raw data into elemental composition and formula was not achieved by simple deduction. Experimental results, including those gained using the *Kaliapparat*, were *not* all equally valid, neither were they straightforwardly replicable.[47] Even once numerical consensus was reached, moreover, these results often remained theoretically ambiguous, only acquiring meaning through interpretation. Far from "mere manipulation", organic analysis using the *Kaliapparat* depended on the analyst's ability to select successful experimental results, and to interpret those results in the light of both vast collective empirical experience of analysis in general and his own understanding of the specific chemical behaviour of the substance being analysed. This philosophy of practice, some aspects of which Liebig codified in his 1837 textbook *Introduction to the Analysis of Organic Bodies* and which he discussed at length in the course of several analytical disputes during the late 1830s, sheds light on some central and hitherto poorly understood aspects of scientific activity. It made explicit, for example, the need for analysts to select data, and it emphasised the importance of managing, rather than eliminating, the uncertainties inherent in the practice of quantitative organic analysis at that time. Both of these features mean that this philosophy of practice challenges widely held notions of the decisive role of experiment in the production of scientific knowledge, so it is particularly significant that Liebig himself not only promoted and defended such behaviour as profoundly scientific but considered it the only means of carrying out true chemical *research* as opposed to mere analysis.

Throughout the 1830s, Liebig taught this approach to his students and assistants in Giessen and strove to propagate it across the European chemical community but by 1839 he was becoming doubtful about the possibility of gaining any secure or lasting theoretical insight into organic chemistry by means of research centred on quantitative analysis. Part of Liebig's response to this was to guide his student Hofmann, then working with the Liverpudlian James Muspratt, to develop the Giessen approach to organic analysis by performing *synthetical investigations*. This approach applied chemical transformations whose constitutional outcome was fairly well understood to relatively simple starting materials. By analysing the products of such reactions Hofmann and Muspratt obtained information from which it was possible to make inferences about the constitution of the starting material. Thus the

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[47] The classic study of experimental replication is Collins 1985.

shift from analysis to synthesis, discussed in Chapter Three, was originally undertaken as a means of constitutional investigation and in the hope of solving dilemmas that Liebig's analytical research programme – for all its achievements – had been unable to resolve. Early synthetic organic chemistry, I argue, was carried out with principally *analytical* goals and not with the aim of constructing organic compounds, whether natural or artificial.

Recovering this original meaning and purpose of synthesis raises some interesting questions concerning existing histories of nineteenth-century organic chemistry, including chemists' histories such as those of Schorlemmer and Graebe mentioned at the start of this *Introduction*.[48] These histories, though they differ in many details, almost all share this feature in common: they entirely ignore any meaning of synthesis other than the purely constructive sense which became dominant around 1880. Synthesis as a tool of analysis is, as I have already mentioned, a recognised eighteenth-century approach to the inorganic world, but there is nothing analogous in the history of organic chemistry – an omission which Chapter Three seeks both to explain and correct. This understanding of the role of early synthetic chemistry in constitutional analysis, moreover, undermines some widely held beliefs about the pre-conditions for successful synthesis. It appears, for example, that chemists in the mid-nineteenth century were frequently in a state of very considerable uncertainty, if not outright ignorance, concerning the identity of their synthetic products. A successful synthesis was, in many instances, the only way to establish a substance's probable constitution, whilst failed syntheses – such as William Perkin's attempted preparation of quinine in 1856 – often produced novel substances whose identities then became the subject of investigation in their own right.

I argue that this question of chemical identity was a major dilemma in nineteenth-century organic chemistry, and I show how chemists developed standardised methods of measuring melting and boiling points as means of deciding whether two substances were the same or different. In a case study spanning Chapters Three and Four I use the alkaloids quinine and coniine to illustrate the problem of chemical identity, the changing role played by synthesis in settling questions of identity and constitution, and how the meaning, purpose and practice of synthesis changed during the second-half of the nineteenth century. The alkaloids, largely because of their remarkable medicinal properties, had been a focus of chemists' analytical attention ever since their isolation in the 1820s, and their synthesis became a matter

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[48] See Bensaude-Vincent (2003) for a recent review of approaches to writing the history of nineteenth-century chemistry.

of pressing interest during the mid-century. Synthesis offered the best hope of confirming chemists' provisional views regarding their constitution, and medically important alkaloids such as quinine were quickly recognised as commercially desirable targets for constructive synthesis. Quinine, however, proved more than a match for mid-nineteenth century chemists, leading to their pursuit of two complementary subjects of investigation: artificial nitrogenous bases including aniline, and somewhat simpler natural alkaloids such as coniine.

I explore the relationship between Hofmann's constitutional investigation and preparation of artificial nitrogenous bases, and his dogged commitment to the possibility of preparing natural alkaloids including quinine by synthesis. In the end, the constitutionally less complex coniine, the toxic active constituent of hemlock, was the first natural alkaloid to be synthesised. Even in this case, however, a period of fifteen years elapsed between Hugo Schiff's first claim to have synthesised coniine and its successful synthesis by Ladenburg in 1886. I examine the role played by Schiff's failed synthesis in prompting Hofmann to take up the constitutional analysis of coniine, and I explain why it was Ladenburg and not the eminent, vastly more experienced and much better placed Hofmann who succeeded in synthesising coniine. My account of the constitutional analysis and eventual synthesis of coniine exposes the gulf between the experimental practices of Hofmann and Ladenburg. Whereas Hofmann continued to see synthesis primarily as a means of solving broader chemical questions, his approach to research still incorporating essential elements of the philosophy of practice he had learnt from Liebig, Ladenburg's work on the synthesis of coniine had much more restricted objectives. Hofmann's research certainly benefited from the very considerable resources of his Berlin laboratory but I claim that the younger Ladenburg succeeded *because* he focused on the specific goal of constructive synthesis, thereby limiting the extent to which theoretical questions impinged upon his work. In pursuing the synthesis of coniine, moreover, Ladenburg made two significant advances in chemical practice, both of them dependent on the innovative use of chemical glassware, and the balance of Chapter Four examines chemists' increasing reliance on glass apparatus and glass blowing and their crucial role in the practice of synthetic organic chemistry.

Doing constructive synthesis involved the application of new experimental procedures on an enormous scale. As a result, both the number of chemists being trained and the nature of the training they received changed substantially during the second-half of the nineteenth century. In my fifth and final chapter, I show how

these factors drove chemists to transform their laboratory environment. Where previously academic chemical laboratories had been created within whatever buildings were made available by the university, from the mid-1860s they were purpose-built to the specification of chemists like Hofmann. Maintaining chemistry's academic credentials was partly a matter of promoting its scientific status, but it was just as important to manage the risks posed by training large numbers of young chemists to perform potentially dangerous manipulations. The new chemistry set gave skilled chemists unprecedented levels of control over chemical processes, but the combination of extremes of temperature and pressure with the often unpredictable properties of the products of synthesis was inevitably hazardous.

Fine speeches and grand buildings were powerful propaganda but only the imposition of tight discipline and structured training through the design and construction of the laboratory enabled organic synthesis to conform to the scholarly ideals of the university. In Chapter Five I argue that the institutionalisation of organic chemistry in late-nineteenth century Germany cannot be understood without considering what was going on *inside* the laboratory. It is, however, an equally important outcome of this history that the practice of organic synthesis could not have developed within universities without the institutional laboratories designed by late-nineteenth century chemists. In concluding my study I propose that it is these laboratories – rather than Liebig's Giessen laboratory – which formed the archetype of the twentieth-century chemical laboratory. I argue, finally, that this revised view of the institutionalisation of chemistry has important implications for our understanding of what has been dubbed the *institutional revolution*, both within chemistry and across the disciplinary spectrum of late-nineteenth century science.[49]

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[49] The term "institutional revolution" was introduced by Cahan 1985.

# Chapter One: The View from Giessen

> *[I]n order to exert a permanent influence in a large circle one must be at the top of a school ie one must be able to educate pupils who understand us [sic] and who have the ability to bring the seed sown amongst them to development.*
>
> *Justus Liebig (1846)*[50]

## Introduction

There are few aspects of the history of chemistry so well studied as the triumphal rise of Justus Liebig. From the late-nineteenth century onwards, accounts of Liebig's life and work have emphasised his two-fold scientific legacy: the foundation of the Giessen school, which transformed the training of chemists; and his introduction of a new piece of apparatus – the *Kaliapparat* – which solved the pressing problem of quantitative organic analysis (Figure 1).[51] In the 1875 Faraday lecture *The Life-work of Liebig*, for example, his most eminent pupil August Wilhelm Hofmann explained that Liebig had not only "given us the instruments and the means of prosecuting the researches by which the domain of chemistry must be enlarged; but he has also shown us how to keep up the supply of intellectual agents to carry on the work ... furnishing trained soldiers to wield the arms he previously provided".[52]

Our knowledge of Liebig's life and work has been greatly increased by Frederic Holmes' insightful and extensive entry in the *Dictionary of Scientific Biography* and by William Brock's more recent and much more comprehensive biography, but

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[50] Justus Liebig to Prof. Dr. [Matthias Jacob] Schleiden, [Professor of Physiology] at Jena, 16 July 1846. Letter in the collection of Assorted Letters (1818-1961) held in the library of the Royal Society of Chemistry, London.

[51] The new apparatus was first referred to as the *Kaliapparat* in the Liebig-Wöhler correspondence, letter 74, Wöhler to Liebig, [29] January 1832, the term being in widespread use from about 1833. A variety of other names – including *(Fünf)kugelapparat* and *Kugelröhren* which reflected its form – remained in common use thereafter. In English Liebig's apparatus was commonly known as the *potash apparatus* or *potash bulbs*. I have chosen to use the term *Kaliapparat* throughout this thesis except where other terms are used in direct quotation. The *Kaliapparat* was a small piece of glass apparatus normally containing a solution of caustic potash to absorb the carbon dioxide produced by burning an organic substance. Determining the increase in mass of the *Kaliapparat* during a combustion analysis gave a direct, gravimetric measure of the carbon content of the sample. The Liebig-Wöhler letters (referred to hereafter as L-W) are cited from new transcriptions of the entire correspondence being made by Christoph Meinel at the University of Regensburg. I am grateful to Professor Meinel for allowing me to use this currently unpublished material. Throughout this dissertation, translations are my own except where otherwise stated.

[52] Hofmann 1876, 8. The classic biography of Liebig is Volhard 1909. Volhard was a student and relative by marriage of Liebig.

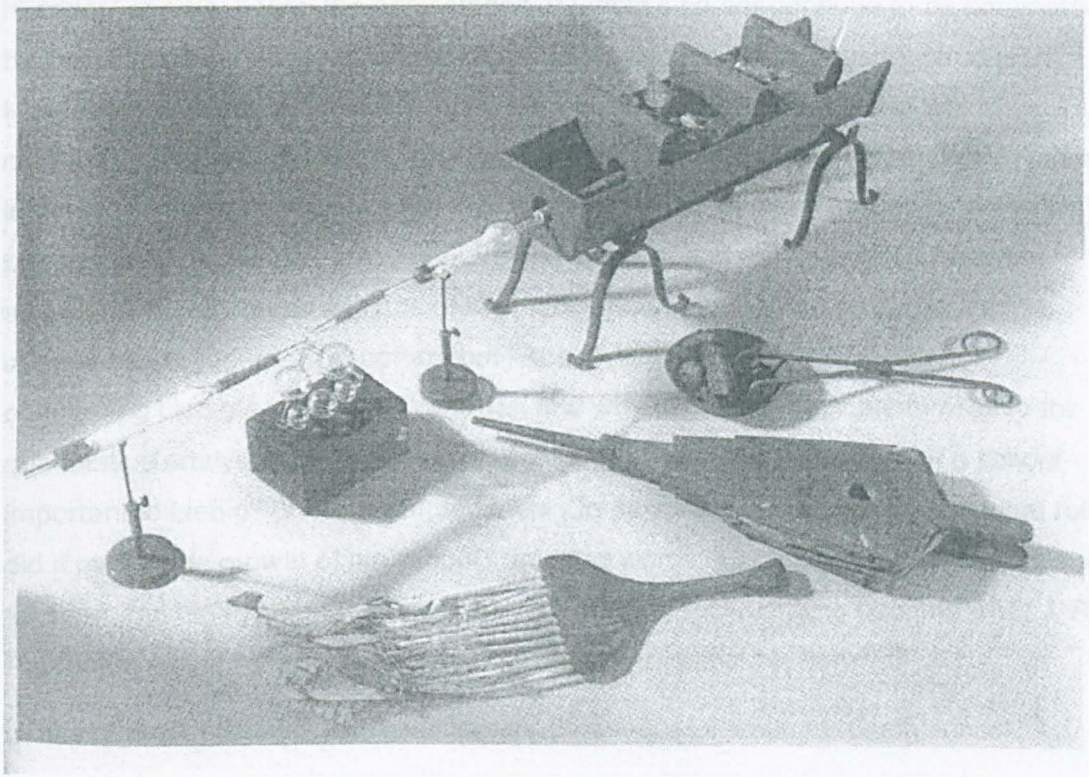

Figure 1. This reconstruction of Liebig's apparatus for organic analysis as it existed around 1840 includes a modern *Kaliapparat*, supported on a wooden block, between two calcium chloride tubes. Water vapour was absorbed by the calcium chloride, whilst caustic potash solution in the *Kaliapparat* trapped carbon dioxide gas. (Deutsches Museum, Picture 1732.)

historical approaches to the early stages of Liebig's career continue to be dominated by the elements – research school plus *Kaliapparat* – which Hofmann introduced.[53] Historians have struggled to reconcile the incomparably high regard in which chemists have held Liebig since the late-nineteenth century with his relatively limited lasting theoretical contributions to the discipline, and they have tended to stress his pedagogical innovations as a result.[54] This chapter and the one which follows address precisely these aspects of the Liebig story, but they do so in order to answer what I regard as important but hitherto largely neglected questions concerning Liebig's chosen path. When and why did Liebig dedicate himself to the quantitative analysis of organic substances? Why was the foundation of a school important to Liebig? What prompted Liebig to develop the *Kaliapparat* and what role did it play in the growth of his school? In other words, just how *did* an ambitious and talented, but highly-strung young man from modest social origins become what J. R. Partington called "unquestionably the greatest chemist of his time"?[55]

In this chapter I discuss the development of Liebig's Giessen research school, concentrating on the relatively little studied period before 1835.[56] I begin by challenging two aspects of the standard account of the early history of the Giessen school: first that Liebig's desire to have his own school was unusual and somehow prescient; and second that his focus on organic analysis is not in need of historical explanation. Although the first point has attracted quite a lot of historical comment, this has mainly concerned the extent of originality of the system of training Liebig introduced in Giessen compared with earlier pharmaceutical training schools including those of Johann Trommsdorff and Friedrich Stromeyer.[57] Historians' failure to examine the second question, meanwhile, probably derives largely from

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[53] Holmes 1973; Brock 1997. The term "research school" was first applied to Liebig's Giessen school by Morrell 1972.

[54] Liebig's first English-language biographer William Shenstone (1902) wished to correct "the prevailing impression concerning Liebig" that "he was a man who made a large fortune by making 'extract of meat'" (p. v) and to revive knowledge of Liebig's "half forgotten" educational work (p. 10). Subsequent historians from Partington (1964, 298) and Morrell (1972, 2) onwards have considered his experimental establishment (with Wöhler) of the radical theory to be Liebig's most significant contribution to the development of chemical knowledge. Even Holmes (1973, 344) considered that: "Few of his theories were highly original, and none of them definitive."

[55] Partington 1964, 300. On Liebig's social rise, see Munday 1990.

[56] In addition to Morrell 1972, classic studies of Liebig's Giessen research school are: Fruton 1988; and Holmes 1989. Any attempt to study the early development of the Giessen school must differentiate carefully – as Fruton did – between the original 1825 school for pharmacy and the smaller group of young chemists who studied and collaborated with Liebig from the late 1820s onwards in the field of organic analysis, and so I emphasise that the latter is my interest here.

[57] See Homburg (1999) on Stromeyer's laboratory in Göttingen, and Rocke's (2003) response.

Liebig's later suggestion that his interest in organic analysis was a direct result of learning, using and developing the method in Gay-Lussac's Parisian laboratory during the spring of 1824 even though, as I discuss below, Liebig did not focus his research in the area of organic analysis until the late 1820s.[58] Undermining these standard elements of the Liebig story is significant in this history because it re-opens important questions about the foundation of the Giessen school and the direction of Liebig's research. If founding a school was not in itself such a remarkable act, then what features of the Giessen school made it so special? And if quantitative organic analysis, in particular the analysis of the nitrogenous organic bases now known as *alkaloids*, was not simply the obvious research problem, then why did Liebig choose to focus his work in this demanding and difficult area?

It is worth noting at this point, although this is dealt with in more detail in Chapter Two, that Liebig's famous alkaloid analyses – published together with his introduction of the *Kaliapparat* in 1831 – in no sense *solved* the problem of analysing alkaloids.[59] These substances, many of which had been isolated from plants during the 1820s by Parisian pharmacists, were of great interest because of their remarkable medicinal and physiological properties, but they were also extraordinarily challenging subjects for the emerging practice of quantitative organic analysis, mainly because they contained nitrogen in extremely small quantities.[60] There is, furthermore, no evidence that Liebig directed any student in Giessen to perform the analysis of an alkaloid at any time, even after the introduction of the *Kaliapparat*. His 1837 *Introduction to the Analysis of Organic Bodies*, on the contrary, suggests that the analysis of nitrogenous substances was not a suitable task for students.[61] We know, moreover, that Liebig regarded the new alkaloid analyses published in 1838 by Victor Regnault – who had previously studied with Liebig in Giessen – as utterly pointless because it *remained impossible* to achieve any certainty about the composition of substances like morphine and quinine by means of quantitative organic analysis.[62] It is therefore unreasonable to sustain any notion that Liebig's alkaloid analyses were pursued with an explicitly pedagogical project in mind, which leaves us without a plausible explanation for either the

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[58] Volhard 1909, 58. See also Liebig 1926 [1890], 18-20.
[59] Liebig 1831b.
[60] See, for example, Pelletier and Caventou (1820) on the isolation and chemical analysis of quinine.
[61] Liebig 1837b.
[62] Regnault 1838; and Liebig 1838a.

direction of Liebig's own research, or how quantitative organic analysis came to appear to him as a suitable vehicle for large-scale practical training in chemistry.

A central claim of this chapter is that early rivalry with the Parisian chemist Jean Baptiste Dumas was a major factor in Liebig's decision to concentrate his research effort in the area of organic analysis. Whilst Liebig struggled to establish himself in Giessen, his near-contemporary Dumas enjoyed every possible advantage Paris had to offer a young chemist. Liebig's gaze was frequently directed towards Paris during this period: it was where he believed the most interesting chemistry was being done and he was eager for the recognition of Parisian chemists. I claim that the young Dumas was his natural rival and I argue that Liebig was motivated to tackle the analysis of alkaloids in order to demonstrate the superiority of his own analytical skill over Dumas'.

Historians have tended to infer from Liebig's later success in teaching this technique to young chemists that organic analysis using the *Kaliapparat* was relatively easy, and that this simplicity therefore extended to his original alkaloid analyses. I have already indicated, and will demonstrate more fully in Chapter Two, that the alkaloids presented a significant technical challenge to contemporary organic analysis, and I will also show there that Liebig struggled to obtain results he regarded as theoretically informative regarding nitrogen's role in the basicity of the alkaloids even *after* his introduction of the *Kaliapparat*.[63] In this chapter, meanwhile, I use his correspondence with Berzelius and Wöhler to show that both Liebig's alkaloid analyses and his establishment of a research school based on using the *Kaliapparat* to analyse simpler organic substances were achieved at very high personal cost. Liebig suffered severe mental and physical strain throughout the period up to at least 1835 and I claim that letters exchanged between Liebig, Berzelius and Wöhler performed a crucial role in preserving Liebig's emotional stability.[64] Certainly, the Liebig who emerges from these letters is far removed from the brilliant, domineering and belligerent chemist we have come to know from previous studies and this Liebig, I suggest, is unlikely to have been successful without the emotional and practical support he received from these two men.

Both his antagonism towards Dumas and his friendly, almost familial relationships with Berzelius and Wöhler show that Liebig was not working in a social vacuum in

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[63] Liebig hoped, amongst other things, to elucidate the relationship between the nitrogen content of the alkaloids and their ability to saturate acids.
[64] The Liebig-Berzelius correspondence is taken from Lewicki's (1991) reprint of Carrière (1898).

Giessen. Many historians have noted that Liebig was sensitive to criticism, often responding in ways they have tended to characterise as inappropriate and even ungentlemanly.[65] Such commentary, I think, underestimates what was at stake for Liebig in those exchanges. The good opinion of other chemists, particularly established, influential men, was of enormous importance to him, but this was far from being merely a question of personal vanity. Liebig may well have been an arrogant man, but he was also engaged in an all-consuming struggle to establish his own reputation and that of his Giessen school in the eyes of the European chemical community. I argue that accomplishing that goal was not simply a matter of *individual* success, it was something Liebig regarded as essential to the future of the entire *discipline* of organic chemistry and he mobilised every resource at his disposal in Giessen towards this end. Re-construing the Liebig of this period as a participant in an essentially communal practice therefore implies a profound revision of the origins and purpose of the Giessen research school, and it is to this that I devote the final section of this chapter.

## Why Found a School?

> *I have made up my mind to dedicate myself completely to the profession of teaching, Kastner himself has roused me to this, I am awakening as if to a new life as I now see before me the goal that I shall strive to reach. ... Since chemistry and physics are not university subjects I will for a time occupy myself with lecturing on experimental chemistry in Darmstadt, and if my lectures are well received, I shall easily receive an offer to a university; or else it will be possible, in association with other men, as Kastner especially wishes, to found an Institute like that of Trommsdorff, which the state will certainly support in all possible ways.*
>
> *Justus Liebig (1821)*[66]

> *I have no great desire to go to Giessen, I would prefer a position in Darmstadt, in the medical college or in some other suitable place. I wish to know about it, so that I may all the more securely devote myself completely to a branch of chemistry and natural science and in this way meet the requirements of the position. There are so many branches of chemistry, which this includes; as a result the choice will not be difficult.*
>
> *Justus Liebig (1823)*[67]

It is more than thirty years since Bernard Gustin first drew attention to the likely role of Trommsdorff's pharmaceutical institute at Erfurt as a precursor to the Giessen teaching laboratory.[68] Liebig's correspondence (first epigraph) provides explicit support for Gustin's proposal, which has now largely displaced the earlier view that

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[65] See, for example, Holmes 1973, 337; and Partington 1962, 299.
[66] Liebig to his parents, 18 November 1821 from Erlangen. Berl 1928, 30, in the translation from Holmes 1989a, 123-4. Kastner was Liebig's first mentor.
[67] Liebig to his parents, 30 March 1823 from Paris. Berl 1928, 52.
[68] Gustin 1975.

Liebig's plan to found a teaching laboratory was primarily a result of studying chemistry in Paris.[69] As my second epigraph shows, however, time in Paris considerably modified both the type of position and the kind of institutional affiliation Liebig sought. In this section I use a comparison of Liebig's Parisian experience with that of Eilhard Mitscherlich to argue that by the time he arrived in Giessen Liebig was envisaging a teaching institution unlike any then in existence in Germany.

Mitscherlich, in Paris around the same time as Liebig, was deeply impressed by the teaching laboratory at the *École Polytechnique*. He wrote to his former teacher Berzelius in January 1824 saying, "I am certain that a similar arrangement to the teaching laboratory is one of the greatest needs for us in Berlin", continuing to pledge that he would "make all possible efforts" to achieve this end on his return.[70] Exposure to Parisian pedagogical methods had a similar effect on both Liebig and Mitscherlich, which alters our view of Liebig's achievements in several ways. For one thing, it suggests that the *École Polytechnique* (and Thenard's laboratory at the *Collège de France*[71]) may have provided Liebig with more of the plan for his pedagogical approach than is now generally admitted. If, moreover, Liebig's desire to found a school was not a unique insight into the probable means of advancing German chemistry, then we are faced with the questions: why was Liebig so successful where Mitscherlich failed; and what purposes did Liebig envisage such a school would serve?

According to his son Alexander, Mitscherlich was ultimately unsuccessful in establishing a teaching laboratory because of the reluctance of the Prussian ministry to commit funds to the enterprise.[72] We know that Liebig himself considered Prussia's attitude to chemical education to be particularly backward, but we also have evidence that one of Liebig's motivations for setting up a training school for pharmacy was to *supplement* the stipend from his university appointment. Gaining official recognition and financial support for the Giessen school required years of lobbying on Liebig's part and was only achieved in 1833, by which time Giessen was already becoming famous for training chemists in organic analysis.[73] There is nothing to indicate that Liebig enjoyed more state or university support than Mitscherlich until *after* his private school for pharmacy had developed to include

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[69] Holmes 1989, 122-4. See also Rocke 2001, 31.
[70] Mitscherlich to Berzelius, Paris, 16 January 1824 in Söderbaum 1932, 39.
[71] García-Belmar 2006.
[72] Mitscherlich 1896a, 11.
[73] Liebig 1840a; Turner 1982. See also Brock (1997, 57-59) on the amalgamation of Liebig's private school with his official university teaching in 1833, and on his struggle to obtain increased support from the state of Hessen.

methods of training and forms of chemical investigation which were demonstrably productive in ways seen as appropriate to the academy.

We also know that Liebig was desperate to continue chemical investigations of the kind he had witnessed and participated in whilst in Paris. Mitscherlich on the other hand – partly as a result of loyalty to Berzelius and his experimental methods, and partly because he remained excluded from *élite* Parisian laboratories – found little to admire in Parisian chemical research.[74] The foundation of a school, I suggest, offered Liebig a possibility which did not interest Mitscherlich, who was then Professor of Chemistry at the University of Berlin and director of the chemical laboratory in the *Dorotheenstrasse*. In the first instance such a school would serve as a useful source of supplementary income but, at least as important to Liebig, this financial resource when combined with the school's laboratory facilities and students had the potential to support investigative chemistry. Whereas Mitscherlich admired and probably wished to emulate the provision of state-funded chemical training at the *École Polytechnique*, Liebig realised that strenuous entrepreneurial activity might make it possible for him to create suitable conditions for chemical research in the less favourable environment of provincial Germany.

I argue that the question of *what* such a school might investigate remained open in Liebig's mind for rather longer than most previous historians have acknowledged. As the epigraphs to this section indicate, Liebig's expressed commitment to teaching substantially predated his choice to specialise in a particular branch of chemistry. Even after his arrival in Giessen, moreover, Liebig did not immediately devote himself to organic analysis. His published research output ranged widely during the 1820s, only including organic analyses from 1826 onwards and only becoming concentrated in this area around 1830. Liebig's early publications and his correspondence with chemists including Berzelius and Wöhler show that he was interested in inorganic chemistry and remained so throughout the 1830s. It does not appear to have been self-evident to the young Liebig that research in the area of organic analysis was the way to forge a career. Deciding to make organic analysis the focus of his personal research, and realising that it could form the experimental core of a productive research programme in the hands of relatively inexperienced chemists in his school were critical steps in Liebig's rise to eminence which have,

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[74] In an interesting contrast with Liebig's experience, Mitscherlich expressed the view that there was not much concerning the accuracy of analysis or chemical investigations that he could take with him from Paris. See Mitscherlich to Berzelius, Paris, 16 January 1824 in Söderbaum 1932, 39.

until now, been obscured by the standard narrative in which it is often assumed that Liebig founded a research school *for* organic analysis, and that he invented the *Kaliapparat in order to* make such a school viable.[75] Even Holmes, though he recognised that the origins of Liebig's research school predated both Liebig's commitment to organic analysis and his introduction of the *Kaliapparat* as a tool for research in that area, provided no detailed historical explanation for Liebig's move to organic analysis, the creation of his school or his development of a new analytical apparatus.[76] Later sections of this chapter therefore explain how and why Liebig's research became concentrated on organic analysis and show how this research produced experience and resources – including the *Kaliapparat* – which were essential to Liebig's development of a pedagogical system by which he was able to transform the labour of his students and assistants into cutting-edge research.

## The Move to Organic Analysis

> *The analysis of quinine and cinchonine etc. produces equally variable results [as for morphine]; indeed one may assert that all analyses of nitrogenous substances, in which the ratio of nitrogen to carbon is more [sic] than 1:5, determined in the usual manner, furnish no reliability.*
>
> *Liebig's (1829) criticism of Dumas and Pelletier's (1823) alkaloid analyses*[77]
>
> *The just trust, which the opinions of this talented chemist deserve, makes it my duty to explain here the facts which I found opportunity to observe on this subject on many occasions.*
>
> *Dumas' (1830) response*[78]

The rivalry between Liebig and Dumas has generally been considered to follow, if not have been caused by, Liebig's commitment to organic analysis, but in this section I argue for a reversal of this relationship. My argument is partly based on a reappraisal of the relative standing of the two chemists, but it also involves tracing the subject and causes of their original disagreements. The disputes between Liebig and Dumas are, of course, extremely well-known in the history of chemistry, where they are usually portrayed as primarily theoretical differences of opinion between equally established chemists whose research programmes overlapped to a considerable extent.[79] Holmes, for example, proposed that the "most compelling explanation" for their disagreements during the mid-1830s was that "Liebig saw

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[75] This view – handed down by Volhard (1909) – remains persistent. See, for example, Levere (2001, 129).
[76] Holmes 1989a, 130-135.
[77] Liebig 1829, 391. N.B. Liebig was referring to the difficulty of determining *low* nitrogen content reliably.
[78] Dumas 1830, 478.
[79] Holmes (1973, 335-344) is an excellent account of the complex theoretical disputes between Liebig and Dumas. Fruton (1988, 8-9) discussed the similarities between the research programmes of Liebig and Dumas.

himself as locked in a titanic struggle with Dumas to direct the development of the field".[80]

I accept this as a fair portrayal of the situation from the mid-1830s onwards, but not before. For one thing Dumas occupied a considerably more favourable position than Liebig during the period up to at least 1832.[81] As Rocke has discussed, the two "apparently ... became acquainted" in Paris where Dumas, who was just a few years older than Liebig, became Thenard's *protégé*.[82] But whereas Liebig was forced to abandon the supportive environment of Gay-Lussac's laboratory to take up his post in Giessen in 1824, Dumas remained in Paris where he continued to enjoy the patronage of the scientific *élite* and freed himself from financial necessity by marrying well.[83] Whilst Liebig struggled to establish himself in Giessen, Dumas' status rose rapidly with the result that he soon came to be regarded as the most influential French chemist of his generation.[84] Seen from Liebig's point of view, I suggest, Dumas at this stage had everything Liebig wanted but did not have.

Moreover, although it is certainly true that Liebig and Dumas disagreed about chemical theory, their early discord in particular was frequently expressed through criticisms of each other's practical techniques, focused mainly on the technically challenging determination of the nitrogen content of organic substances. The origins of this dispute have usually been ascribed to Dumas' response to Liebig's 1831 publication of a series of alkaloid analyses performed using his newly developed *Kaliapparat*.[85] Liebig had analysed the same alkaloids studied by Dumas and Pelletier in 1823, but his results led him to very different conclusions regarding their composition and formulae – particularly with respect to their nitrogen content. In addition to his new apparatus for determining carbon, Liebig's paper described a new approach to measuring the small nitrogen content of substances such as the alkaloids and, as I discuss in detail in Chapter Two, *this* was the aspect of his work which drew most stinging criticism from Dumas.

It has, moreover, not previously been noted that Liebig had become interested in Dumas and Pelletier's alkaloid analyses some two years earlier during his investigation of organic acids found in the urine of grass-eating, four-footed animals.

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[80] Holmes 1987a, 128.
[81] Rocke (2001, 107-108) has suggested that Liebig enjoyed a "far more favourable situation" than Dumas, but there is little evidence to support this claim during the period up to at least 1835.
[82] Rocke 2002, 277.
[83] Crosland 1967, 444.
[84] Rocke 2001, 55.
[85] See, for example, Rocke 2002, 285-6.

At that time, whilst struggling with the accurate determination of the small nitrogen content of hippuric acid (*Hippursäure*) using the existing methods of analysis, Liebig repeated Dumas and Pelletier's analyses of morphine and other alkaloids, which also contain very little nitrogen (see epigraph).[86] He concluded that, just as he had failed to obtain a "decisive result" for the nitrogen content of hippuric acid, so Dumas and Pelletier's result for morphine could not be regarded as reliable.[87] Thus Liebig, in one of his earliest independent publications concerned with organic analysis, chose to challenge work which had been important in establishing Dumas' reputation.

Dumas responded in a paper published the following year, in which he defended both the method he and Pelletier had employed and the results they had obtained. Their results for the analysis of the sample of morphine prepared with magnesium oxide were, he claimed, identical to Liebig's, whilst the difference in the results for the sample prepared with potassium (oxide) might be due to either preparation or analysis. He concluded his refutation of Liebig's criticisms with the rather condescending comment reproduced in the epigraph.[88] Dumas' response to Liebig's criticisms may have been based on inconclusive arguments, but it also contained a clear claim to superior knowledge and experience. I suggest that such a dismissal struck a serious blow to Liebig's desire for continued recognition in Paris and that this slight fuelled Liebig's determination to develop his analytical skill and perform the technically immensely difficult analysis of alkaloids.[89] In other words, Liebig did not fall into dispute with Dumas as a consequence of his systematic alkaloid analyses; rather, he chose to focus on the analysis of alkaloids in order to settle a score with Dumas.

Liebig certainly began to dedicate more time and effort to organic analysis from this point on, publishing several papers in this area during 1829 and 1830.[90] He also began an unusual collaboration with Wöhler, which can tell us a lot about Liebig's position within the German chemical community and about the relationship between German and Parisian chemistry. Wöhler and Liebig had come to know each other in rather unfortunate circumstances during the mid-1820s, when they disagreed publicly about the analysis of silver cyanate, but by 1830 the two were in regular and

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[86] Dumas and Pelletier's (1823) analyses were carried out using the method developed by Gay-Lussac and Thenard.
[87] Liebig 1829, 390 ("kein scharfbegrenztes Resultat") and 391.
[88] Dumas 1830, 478.
[89] Kim (1996, 7) like Holmes (1973, 331) maintained that Liebig's motivation was primarily theoretical, whereas I claim that this was a secondary factor.
[90] Liebig 1830a and 1830b.

friendly correspondence. Wöhler, an ex-pupil of Berzelius then working in Berlin, had initiated both their correspondence and the idea that they might work together.[91] Wöhler's motivation included a rather light-hearted wish to confound those who saw the two as sworn enemies, but for Liebig the stakes were a lot higher. In agreeing that the analysis of mellitic acid (*Honigsteinsäure*) should be the subject of their first joint publication Liebig suggested to Wöhler – who had not performed any of the quantitative analytical work – that he might reciprocate by publishing "any small piece of work" under their joint names.[92] Liebig was determined that they show a united front "for my friends in Paris believe nothing different than that we live in open feud, and I wish to see this tasteless idea disappear", and he was prepared to sacrifice due recognition for his own work in pursuit of this goal.[93]

When Wöhler first suggested that they work together in the summer of 1829, he left the choice of topic to Liebig. Whether in deference to Wöhler's research interests, or as a way of avoiding the area over which they had previously disagreed, Liebig did not propose an investigation based on quantitative organic analysis. Instead he suggested that they investigate the inorganic compounds of nitrogen by studying the reaction of sulphur chloride (*Chlorschwefel*) with ammonia.[94] Wöhler rejected Liebig's proposal. He refused to work with chlorine or its volatile compounds on health grounds, and suggested they continue his preliminary investigations of mellitic acid.[95] Wöhler was interested in mellitic acid because he suspected that – like oxalic acid – it contained no hydrogen, but he could think of "no other form of proof than copper oxide analysis which I find extremely awkward". He therefore made "the very self-serving suggestion" that Liebig, who was "equipped for it and so practised at it", should carry out the analysis of the acid whilst he provided the material to be analysed.[96]

Much as he had benefited from training with Berzelius and despite his close connections with eminent Berlin chemists including Poggendorff and Mitscherlich, Wöhler recognized Liebig as possessing vastly superior skill and equipment for quantitative organic analysis. By 1829, about the time he first crossed swords with Dumas but well before his introduction of the *Kaliapparat*, Liebig was already known

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[91] L-W, letter 2, Wöhler to Liebig, [20] January 1829. The suggestion that they work together was made in letter 4, Wöhler to Liebig, 8 June 1829.
[92] The joint publication was Liebig and Wöhler 1830a. Wöhler's contribution had been the provision of material to be analysed. See L-W, letter 15, Wöhler to Liebig, 10 February 1830.
[93] L-W, letter 14, Liebig to Wöhler, 28 January 1830.
[94] L-W, letter 5, Liebig to Wöhler, 12 July 1829.
[95] L-W, letter 6, Wöhler to Liebig, 22 November 1829.
[96] L-W, letter 6, Wöhler to Liebig, 22 November 1829.

in Berlin as the most outstanding analyst of organic substances in Germany, and it is reasonable to conjecture that gaining access to this expertise was a significant factor in motivating Wöhler's approach to Liebig. Wöhler's letters, meanwhile, provided Liebig with a valuable link to Berlin chemical circles, keeping him in touch with scientific and social developments in the capital. Joint publication was presumably also advantageous to both men, since they published together several times during the following years – even though, as with mellitic acid, all the quantitative organic analyses they published continued to be carried out by Liebig until after Wöhler learnt to use the *Kaliapparat* during a visit to Giessen in November 1831.[97]

Liebig, meanwhile, continued to develop his skills in organic analysis and when Wöhler suggested in February 1830, shortly after the completion of the mellitic acid paper, that they combine their work on cyanic acid, he responded by proposing a joint investigation of the organic bases previously analysed by Dumas and Pelletier:

> *I am actively convinced that, if little by little we set ourselves various tasks which must clarify important points in organic chemistry, we will thereby produce a revolution. This field is so little studied and certainly more fruitful than it seems. What do you think of the organic bases? I scarcely doubt that the analyses of D[umas] and P[elletier] are incorrect. A single experiment, and that is the determination of their combining weights, would decide. I have it in mind to carry out the experiment, and should it give the hope of finding something new, then we could pursue it.*[98]

Wöhler's reply concentrated on a lengthy report of his most recent investigations of the cyanic acids, and he again rejected Liebig's suggested research topic. He had carried out a variety of experiments on the alkaloids, Wöhler wrote, including attempting their preparation by reacting acids with ammonia but had never studied them by means of quantitative analysis. The implication was that such investigations were likely to be too difficult and, seemingly by default, the cyanic acids became the subject of their next joint publication.[99]

Liebig's letter shows that by the spring of 1830 he felt himself to be in a position to challenge Dumas' claimed superiority in organic analysis, and particularly alkaloid analysis – even though he might have preferred to do this with Wöhler's help. Since first coming into conflict with Dumas over the analysis of morphine, Liebig had

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[97] Liebig and Wöhler 1830b. See letter 21, Wöhler to Liebig, 5 August 1830.
L-W, letter 15, Wöhler to Liebig, 10 February 1830, acknowledged how little Wöhler had contributed to the mellitic acid investigation.
[98] L-W, letter 15, Wöhler to Liebig, 10 February 1830; and letter 16, Liebig to Wöhler, 8 March 1830.
[99] L-W, letter 17, Wöhler to Liebig, 21 March 1830. The resulting publication was: Liebig and Wöhler 1830b.

concentrated his research in the area of quantitative organic analysis, accumulating substantial experience in the process. In addition, and as I discuss later in this chapter, he had begun to teach the techniques of quantitative organic analysis to some of his students in Giessen. Within Germany Liebig was a recognised expert in the field, yet Dumas continued to treat him with indulgent condescension. Wöhler might be unwilling to participate in the venture but Liebig believed the field of organic chemistry was ripe for remarkable discoveries, which he was determined to make. Within six months Liebig had embarked upon the laborious and demanding analyses of the alkaloids, and it was during this work that he developed the *Kaliapparat*. Liebig's personal research was the context for the invention of the *Kaliapparat*, and it thereby provided him with an essential component of the experimental practice on which the subsequent growth of his research school was based.

## Managing with so little

> *Imagine, after great difficulties I could only get a donation [subsidy] of 100 Gulden for the laboratory and for buying instruments, reagents and materials. May Heaven have mercy on me! How can I manage with so little?*
>
> *Justus Liebig (1824)*[100]

By the late summer of 1830, six years after returning from Paris to take up the post of *außerordentlicher Professor* of Chemistry at the University of Giessen, Liebig was poised to tackle one of the central problems of quantitative organic analysis: the analysis of the alkaloids. The question, "How can I manage with so little?" had preoccupied Liebig since his arrival in Giessen, and he had been persistent and ingenious in answering it. His small, poorly equipped laboratory originally lacked the apparatus needed to carry out quantitative organic analysis, but Liebig supplied this want by bringing apparatus from Paris and by returning there to improve his glass-blowing skill.[101] Whereas Liebig had complained in 1828 that he was unable to complete analytical investigations begun in Paris because he lacked suitable equipment, he was now recognised in Berlin as the foremost German practitioner of quantitative organic analysis.[102] The provincial university town of Giessen could boast a school for practical training in pharmacy and chemistry, and this school was now attracting sufficient numbers of students for the fees to make a valuable addition to Liebig's meagre income. Some of his students, moreover, were able and

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[100] Liebig to August Walloth, 23 September 1824 from Giessen, cited in Brock (1997, 40) from Berl (1928, 75).
[101] Brock (1997, 37-8) described the poor state of the provincial University of Giessen in the 1820s.
[102] See, for example, Liebig (1828, 191) on the difficulty of completing analytical research on indigo begun in Paris.

willing to contribute to Liebig's research, thereby providing him with a local chemical community of sorts. Giessen still lacked the financial and material resources characteristic of Parisian science in this period, but Liebig had done a very great deal to improve his lot.

In one important sense, however, Liebig continued to be seriously disadvantaged by his Giessen situation. Despite the embryonic research community within his school and his increasingly intimate correspondence with Wöhler, Liebig otherwise remained socially and intellectually isolated. Above all, he lacked the society of more experienced chemists. Liebig had had no sustained contact with a chemist-mentor since leaving Gay-Lussac's laboratory, and it is reasonable to infer from his repeated return visits to Paris that he felt the lack of such support. Hard work and clever use of the resources available to him had enabled Liebig to overcome most of the limitations imposed by his Giessen location, but he could not recreate the whole range of scientific interactions available to those working in centres of contemporary chemical expertise such as Paris, Stockholm, or even Berlin.

This drawback, which had the potential to drastically limit his success, was removed when Liebig travelled to Hamburg in September 1830, to the *Versammlung Deutscher Aerzte und Naturforscher*, where he met Wöhler's former teacher Berzelius.[103] Liebig declared himself "literally at peace" following the meeting, during which the two had discussed chemistry, including the analysis of the alkaloids.[104] The eminent Berzelius was well placed to understand Liebig's sense of geographical and social isolation and had years of experience practising chemistry with limited material resources. Berzelius invited Liebig to write to him and I contend that this correspondence, together with Liebig's developing and mainly epistolatory relationship with Wöhler, was of great significance to the young Liebig. These well documented friendships-at-a-distance seem largely to have fulfilled Liebig's need for social and scientific companionship. In addition to advising on scientific and professional matters, Berzelius helped Liebig to preserve his fragile emotional stability during periods of intense hard work and frustration, whilst Wöhler gave Liebig an outlet for his less guarded outpourings of unhappiness and fatigue. The close friendship between Berzelius and Wöhler, meanwhile, ensured that the two were able to act in concert and I argue that their support, though almost entirely

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[103] L-W, letter 19, Wöhler to Liebig, 26 July 1830; and letter 20, Liebig to Wöhler, [4] August 1830. This was the only meeting between Liebig and Berzelius.
[104] L-W, letter 30, Liebig to Wöhler, 12 October 1830.

provided through the medium of letters, was nevertheless essential to Leibig's early success in both scientific and psychological terms.[105]

Liebig first wrote to Berzelius in January 1831, and he was overjoyed when the older man replied swiftly and encouragingly.[106] Liebig had implored Berzelius to respond as quickly as possible to his new method of analysis, including the use of the *Kaliapparat*, then just about to be published in Poggendorff's *Annalen der Physik und Chemie*. Berzelius did not address Liebig's analytical work at first, deferring this topic until his second letter, written a couple of months later. By this time, Berzelius had received Liebig's article from Poggendorff and included a description of the new method in his *Jahres-Bericht* for 1831 and in his textbook.[107] Berzelius' letter contained a very positive assessment of Liebig's work, though he remarked upon a few erroneous figures, which he politely attributed to the printing process.[108] Berzelius had previously expressed concern in his correspondence with Wöhler at the negligence of Liebig's analyses, but he had also acknowledged Liebig's hard work and clear thinking.[109] Whatever his earlier doubts about the accuracy of Liebig's work, Berzelius now chose to emphasise Liebig's productivity. "I find it utterly inconceivable", he marvelled, "how you have been able to carry out all these things in such a short time".[110]

Liebig was delighted by Berzelius' reception of his analyses, which he considered "the loveliest reward, the most satisfying compensation ... for the unspeakable effort, which this work has cost me". The suggestion that he should pursue the analysis of the alkaloids in order to discover more about the general features of their composition was rather less welcome, prompting Liebig to complain that "these experiments were so laborious, that they drove me to despair". Following five months' uninterrupted work on the determination of nitrogen, at the end of which he remained dissatisfied with this component of his method of analysis, Liebig felt that

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[105] The three sets of correspondence, between Liebig and Wöhler, Liebig and Berzelius, and between Wöhler and Berzelius, have been heavily used as valuable resources for the study of chemical theory. See, for example, Holmes' (1964, lviii-lxv) discussion of Liebig's falling out with Berzelius in the early 1840s following the publication of *Animal Chemistry*.
[106] Liebig's first letter to Berzelius was dated 8 January, 1831. Berzelius' initial response was dated 11 February. See Lewicki 1991, 6-7.
[107] Berzelius' second letter to Liebig, 22 April 1831 in Lewicki (1991, 7-8) reported that Berzelius had sent an extract of Liebig's paper to Paris for inclusion in his textbook. See also Berzelius 1832.
[108] Berzelius to Liebig, 22 April 1831, in Lewicki 1991, 7.
[109] Berzelius to Wöhler, 9 July 1830 in Wallach 1901, 304. See also Rocke (2002, 279) on Berzelius and Wöhler's disapprobation of the style of investigation that Liebig had acquired in Paris.
[110] Berzelius to Liebig, 22 April 1831, in Lewicki 1991, 6.

"the courage to do it has completely departed me".[111] Berzelius subsequently urged Liebig to add a "necessary appendix" to his work by analysing the sulphates of the alkaloids, but I have no evidence that Liebig revisited the analysis of the alkaloids until 1838, when his results were again challenged from Paris, this time by his ex-student, Victor Regnault.[112]

By the end of 1831, Berzelius stood in the role of mentor to Liebig, who wished "to seek his advice on a multitude of subjects".[113] Berzelius frequently encouraged Liebig to circumspection, for example in his disputes with other chemists including Carl Löwig and Mitscherlich, but the two were united in their disparaging opinion of the new generation of French chemists in general and of Dumas in particular. Berzelius considered Liebig's alkaloid analyses to have exposed the unreliability of Dumas and Pelletier's results, which was "a damned curious thing". According to Berzelius, the "lovely agreement" in the French results made it evident that Dumas had "helped the results along with the pen".[114] Liebig needed little encouragement to join the attack on his rival. Following Berzelius' lead, Liebig asserted that "the pen had clearly made the greatest contribution" to Dumas' successes. Famously, he likened Dumas to a tightrope walker and gave vent to his intense frustration at the Frenchman's uncanny ability to produce "masterpieces from his sleeve".[115] Liebig's distrust of his rival's results and methods was supported and enhanced by Berzelius.

Berzelius repeatedly expressed concern at Liebig's heavy workload, for example when he warned that the work associated with Liebig's co-editorship of Geiger's *Magazin für Pharmacie* would be fruitless.[116] Liebig was undeterred by Berzelius' suggestion that it would be difficult to obtain interesting material for publication because there were already plenty of good journals in existence. In response, he asked Berzelius to send him both articles and interesting samples for analysis by members of the Giessen research school.[117] Liebig claimed that his main motivation for taking on the work was financial but he nevertheless astutely exploited the opportunity this new role presented. He re-named the *Magazin* the

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[111] Berzelius to Liebig, 22 April 1831, in Lewicki 1991, 7-8. Liebig to Berzelius, 8 May 1831, in Lewicki 1991, 9-10.
[112] Liebig to Berzelius, 8 May 1831 in Lewicki 1991, 10. Berzelius to Liebig, 13 Dec 1831, in Lewicki 1991, 21. Regnault 1838; Liebig 1838a. Regnault's analyses are discussed in Chapter Two.
[113] Liebig to Berzelius, 28 December 1831, in Lewicki 1991, 24-5.
[114] Berzelius to Liebig, 22 April 1831, in Lewicki 1991, 7.
[115] Liebig to Berzelius, 8 May 1831, in Lewicki 1991, 11.
[116] Berzelius to Liebig, 28 Juli 1831, in Lewicki 1991, 13.
[117] Liebig to Berzelius, Beilage zum Brief vom 4. August 1831, in Lewicki 1991, 17.

*Annalen der Pharmacie* in February 1832, and rapidly transformed it into the exclusive organ of publication for analyses carried out in his laboratory. Berzelius provided material for publication in the *Annalen* on only a few occasions, but the detailed descriptions of his research Liebig included in his letters often provided Berzelius with material for inclusion in the *Jahres-Berichte* and new editions of his textbook.[118] Not only did this present Liebig's work to a wider audience, it also provided valuable endorsement from an established and highly respected chemist.

Berzelius' fears proved justified when relentless overwork began to take its toll on Liebig's physical and emotional health. In May 1832, just returned from travelling with Gay-Lussac's son Jules, Liebig wrote to Wöhler:

> *unfortunately my physical condition has been so unbearable throughout the entire holiday period, that I cannot say I was happy to be in my hometown; I had to avoid all company, in order not literally to consume myself, because even the smallest carelessness left me paying for it for days. I won't tell you how it looks regarding sense of humour. In short, I am almost tired of life and can imagine that shooting oneself to death or cutting one's throat are in some cases cooling means. The least spiritual exertion exhausts me so, that I must give it up completely.*[119]

This outpouring seems to have been cathartic, and before continuing to more mundane matters Liebig sought forgiveness: "My dear friend, I feel better already".[120] Responding to this letter, Wöhler diagnosed "Hysteria chemicorum", a "specific illness of the chemist" caused by mental effort, chemical ambition and exposure to chemical vapours and smells. "All great chemists probably [suffer from it]", Wöhler reassured him. According to Berzelius, Wöhler reported, "The man [Liebig] works too hard; he should travel during the summer months".[121]

Wöhler's letter may have encouraged Liebig to adopt a more measured tone in his next letter to Berzelius. "My last piece of work on alcohol has, as always happens to me at the end of a piece of work, made me ill again for a long time", he reported, but he concluded more optimistically by confirming his intention to visit Berzelius in Stockholm.[122] Berzelius was delighted, first suggesting that Liebig travel to Sweden with the recently widowed Wöhler and then, after Liebig proposed delaying the visit,

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[118] Berzelius to Liebig, 21 Mai 1833, in Lewicki 1991, 58-60, contained an extensive description of his investigations of Quellsäure, which Liebig to Berzelius, 30 Mai 1833, in Lewicki 1991, 66, requested permission to publish. On the reverse direction see, for example, Berzelius to Liebig, 11 February 1831 in Lewicki 1991, 6. Berzelius' very first letter encouraged Liebig to send him an account of his analytical results for inclusion in the new French edition of his textbook on plant chemistry.
[119] L-W, letter 84, Liebig to Wöhler, 1 May 1832.
[120] L-W, letter 84, Liebig to Wöhler, 1 May 1832.
[121] L-W, letter 87, Wöhler to Liebig, 16 May 1832.
[122] Liebig to Berzelius, 30 May 1832, in Lewicki 1991, 29, and 31.

extolling the virtues of a Swedish winter: "We should work, joke, ride in a sleigh, not exert ourselves and still produce something".[123] Despite Berzelius' encouragement, the planned visit was repeatedly postponed by Liebig. At the end of 1833, for example, he explained that he was so unwell that his doctor and his wife forbade him to make the journey to Stockholm.[124]

Liebig continued to complain of ill health, whose physical symptoms he attributed to the poor laboratory facilities in Giessen, but his letters also betrayed severe emotional strain.[125] In one outburst, written to Berzelius during the summer of 1834, Liebig compared the sufferings of the chemist with the "pure and unclouded happiness" experienced by woodsmen at the end of a day's work.[126] As Berzelius advised in the spring of the following year, Liebig was simply working too hard: "It is impossible that a nervous temperament should not become exhausted by such assiduous and momentous occupation."[127] Throughout the first half of the 1830s, Berzelius responded patiently to Liebig's concerns, applauded his achievements and consoled him in times of distress. Early in 1836, Liebig expressed the hope that he might return to full health "provided that no emotional excitements and disturbances get in the way", and I deduce that his health improved somewhat since it was not discussed by the two men thereafter.[128]

These letters confirm the high cost Liebig paid for success. Forced by circumstances to rely on a geographically dispersed chemical network, Liebig committed to paper much that would otherwise have passed unrecorded. He vented anger, anxiety and frustration at the same time as he chronicled his chemical achievements. He was producing good work at a staggering rate but the young Liebig, we learn, was often unwell, insecure and in need of reassurance. He benefited from Berzelius' guidance, both scientifically and professionally, whilst Wöhler's friendship provided him with an important emotional outlet, but more than anything else we learn that Liebig realised his ambitions through years of unremitting work. Far from achieving instant success and recognition following the publication of his alkaloid analyses in 1831, Liebig was then merely at the start of an intense struggle to establish himself, his Giessen laboratory and his method of

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[123] Berzelius to Liebig, 22 June 1832, in Lewicki 1991, 31. Liebig to Berzelius, 2 July 1832, in Lewicki 1991, 33. Berzelius to Liebig, 25 July 1832, in Lewicki 1991, 35-36.
[124] Liebig to Berzelius, 14 September 1833, in Lewicki 1991, 72.
[125] Liebig to Berzelius, 14 September 1833, in Lewicki 1991, 68.
[126] Liebig to Berzelius, 22 Juli 1834, in Lewicki 1991, 94.
[127] Berzelius to Liebig, 10 April 1835, in Lewicki 1991, 104-5.
[128] Liebig to Berzelius, 23 Februar 1836, in Lewicki 1991, 111-112.

analysis using the *Kaliapparat* as dominant throughout the European chemical community.

## The Origins and Purpose of Liebig's Giessen Research School

> *To build a great palace we require many workmen, masters and journeymen – we require simple instruments.*
>
> *Justus Liebig (1839)*[129]

The preceding sections have presented a substantially revised view of Liebig's early career and work and in this final section I show how these insights prompt, support and even require a new account of the origins and purpose of Liebig's Giessen research school. I have argued that Liebig's focus on organic analysis, and on the alkaloids in particular, was strongly motivated by his rivalry with Dumas and his desire for continued recognition by the Parisian scientific *élite*. I have shown, furthermore, that the *Kaliapparat* was produced in the context of this research, and not with any immediate pedagogical goal in mind. And whereas the foundation and growth of the Giessen research school are widely considered to have been a straightforward consequence of Liebig's introduction of the *Kaliapparat* in the autumn of 1830, I have shown that the period up to at least 1835 was a difficult and demanding one for Liebig. My findings are not easy to reconcile with the standard history established by Morrell and Holmes, not least because they suggest that the use of the *Kaliapparat* did not in fact lead to an instantaneous simplification of quantitative organic analysis which rendered it easily teachable.[130] In what follows, I explain why Liebig had to work so hard to build up his research school based on quantitative organic analysis using the *Kaliapparat* and why, on the other hand, such a school was essential to Liebig's success.

Holmes' study of Liebig's laboratory reported two interesting happenings which took place in Giessen in 1827, and which I argue were a good deal more important and more connected than Holmes indicated. First, Liebig's student Heinrich Buff published the results of some analytical investigations on indigo performed using the apparatus developed by Liebig and Gay-Lussac in Paris in 1824.[131] Later that year, Liebig announced a substantial revision of the curriculum in the Giessen school which required his students to spend the "entire winter semester ... in the chemical laboratory, whereby they must occupy themselves with analytical work from morning

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[129] Liebig (1837a, 192) as translated by William Gregory in Liebig (1839b, 30).
[130] Morrell 1972, 27-8; Holmes 1973, 332 and 1989a, 132.
[131] Buff 1827.

until evening".[132] Holmes asserted that there was "no indication ... that Liebig was consciously redirecting the goals of the institute", but I cannot agree with that assessment. Despite Buff's somewhat unusual characteristics as a student – he had already matriculated in mathematics at Giessen – he does not appear to me to be an "isolated case", as Holmes suggested. Rather, Buff was the first person whom Liebig instructed in the technique of organic analysis using existing methods. As Holmes himself concluded, the experience of teaching Buff made Liebig aware of the "possibilities for instituting such training on a broader basis in the future".[133] Liebig, I claim, realised two things as a result of working with Buff. First, he learnt that the techniques of organic analysis could be taught, so that students would be in a position to increase the research output of his laboratory in that area. Second, he appreciated that much more extensive and systematic training in analysis would be required to fulfil that goal. I argue that this experience, which pre-dated the introduction of the *Kaliapparat*, played an important role in convincing Liebig that research in the area of organic analysis could be carried out within an appropriate pedagogical context.

The idea that the Giessen research school developed from 1827 onwards is supported by Joseph Fruton's detailed study of Liebig's research group. Fruton showed, moreover, that Liebig's research group consisted of just eleven people in the period up to 1835, some four years after the introduction of the *Kaliapparat*.[134] According to Fruton, the group's small size partly reflected the relatively small proportion of students studying chemistry rather than pharmacy – despite considerable crossover between students of chemistry and pharmacy in this period.[135] It also tends to confirm my claim that Liebig's introduction of the *Kaliapparat* in 1830 did not immediately lead to rapid and unproblematic expansion of his research school. An examination of the information Fruton provided shows that between 1830 and 1834, Liebig's research group consisted of just seven people, six of whom were actively involved in organic analysis.[136] Those six were (roughly in order of entry to the group): Friedrich Kodweiss, Charles Oppermann, Karl Ettling, Jules Gay-Lussac, Rodolphe Blanchet, and Ernst Sell. Between them, they published seven papers on organic analysis in Poggendorff's *Annalen* in the years

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[132] Liebig 1827a and 1827b. Extracted from Holmes' (1989a, 127-128) translation.
[133] Holmes 1989, 128 ("isolated") and 130 ("possibilities").
[134] Fruton's 1988, 11. Three of these eleven initially matriculated in pharmacy.
[135] Whereas 53 of the 76 students enrolled in that period matriculated in pharmacy, only 15 initially matriculated in chemistry.
[136] Fruton 1988, Appendix I. The seventh Karl Winkelblech matriculated in chemistry in 1832, having worked on cobalt oxides, and went to Marburg to study for his doctorate.

from 1831 to 1834 and several more, including a number of reprints, in Liebig's own journal the *Annalen der Pharmacie* from 1832 to 1834.

These papers did much more than simply increase the volume of organic analysis being carried out in Liebig's laboratory. As his own research became more focused in the area of organic analysis, but still before the introduction of the *Kaliapparat*, Liebig continued to instruct his students in quantitative organic analysis and Kodweiss, like Buff before him, was able to produce publishable results.[137] From 1831 onwards, papers published by members of his research school provided crucial validations of Liebig's new method of analysis using the *Kaliapparat* and were often the means by which important developments in this method were made public. For example, Oppermann's 1831 paper on the composition of oil of turpentine reported analyses carried out using the apparatus developed by Liebig with Gay-Lussac as well as using the *Kaliapparat*, which no paper published by Liebig himself ever did.[138] By 1833 the use of the *Kaliapparat* for the determination of carbon had become sufficiently routine in Giessen that it generally no longer warranted a specific mention in published analyses.[139] The assignment of formulae based on such analytical results nevertheless often remained contentious, a state of affairs which Liebig regarded as extremely detrimental to the development of chemical knowledge.[140]

In 1833, Liebig's students Blanchet and Sell published a paper which sought to break that deadlock by unusual means. Echoing Liebig's concern, they described the determination of the laws governing the combining proportions in organic bodies as "the exclusive object of the work of chemists in recent times", explaining that the foundations of a "true system of chemistry" must rest on "an exact knowledge of the composition of organic compounds". They claimed that recent developments in organic analysis, which had rendered it reliable in any hands given care and practice, had enable them to discover the "true composition of organic bodies" by *containing*, rather than eliminating, experimental errors. One of the methods they had used to achieve this involved taking it in turn to repeat analyses until the variation in results was sufficiently small to have no effect on the number of atoms, and hence on the formula assigned to the substance being examined. Although the developments they referred to and the method of analysis they described were due to Liebig,

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[137] Kodweiss 1830.
[138] Oppermann 1831a and 1831b. As I discuss in Chapter Two, though Liebig made many such comparisons he did not publish them.
[139] Liebig himself no longer referred to the method from 1833 onwards.
[140] Liebig 1834a, 47.

Blanchet and Sell did not mention Liebig by name except to thank him briefly for his advice and leadership.[141]

Holmes has examined the essential role of writing up for publication in scientific work.[142] It nevertheless remains unusual to find a scientist explicitly developing this skill in his students. Liebig's encouragement of independent publication by his students has often been interpreted as an altruistic attempt to support their embryonic research careers.[143] The only dissenter was Carl Vogt, one of Liebig's later students, who attributed Liebig's behaviour to a desire to distance himself from his students' mistakes.[144] Blanchet and Sell's paper invites two additional interpretations of Liebig's motivation. One of Liebig's early independent analyses had been of camphor. His results, obtained using the Liebig-Gay-Lussac apparatus, had been challenged by Dumas, becoming a focus of the heated disagreements between Liebig and Dumas during the early 1830s. Blanchet and Sell had also analysed camphor and their results confirmed those obtained by Dumas, refuting Liebig's. In 1833 Blanchet and Sell reported Liebig's explanation of the cause – a problem with the apparatus he had used – and they explained that the same problem had led to substantial errors in the earlier analyses published by Oppermann and Kodweiss, which they also corrected.[145] Liebig used a paper by two of his relatively junior students, both of whom had matriculated the previous year, to avoid having to admit in public that he had been wrong and Dumas had been right.[146]

Blanchet and Sell's paper, like those of Oppermann and Kodweiss before them, also performed an essential role in establishing Liebig's method of organic analysis as trustworthy in the public domain, partly because they gave the impression that the method was in widespread use, but also because they demonstrated its consistency. Whereas previously "different methods produced different results", they claimed that the difficulties of analysis were now confined to those of obtaining organic substances in pure form.[147] Blanchet and Sell had analysed an impressive number of substances, producing convincing analytical data in support of the formulae they

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[141] Blanchet and Sell 1833, 259-260.
[142] Holmes 1987b.
[143] For example, by Morrell 1972, 30.
[144] Fruton (1988, 19) cited Vogt's recollections.
[145] Blanchet and Sell 1833, 304-5.
[146] Liebig was also able to use analyses carried out by his students to challenge published results. For example, in 1834 Liebig used work carried out by Ettling in a critical editorial note to a paper by Dumas in the *Annalen der Pharmacie* concerning the analysis of clove oil. See Liebig's p. 68 footnote to Dumas 1834.
[147] Blanchet and Sell 1833, 260.

assigned. Their paper made explicit in practical terms the futility of pursuing accuracy beyond the point at which formula was determined and the coherence of their results gave credence to the formulae they proposed. Whereas other chemists involved in organic analysis, including Mitscherlich and William Prout, persisted in the belief that achieving the greatest possible accuracy of experimental results was necessary to solving the problem of organic analysis, Liebig's students proposed that what was at stake was the reliable determination of formula. This key strategic move, in which his students Blanchet and Sell played an essential role, enabled Liebig to shift analytical emphasis from the experimentally determined percentage composition to the number of atoms (or equivalents) of each element providing the best theoretical match to the available data. Liebig's early appreciation that reliable and sufficient, rather than maximum, experimental accuracy should be the goal of organic analysis was vital to his success because it re-fashioned the practice of analysis as an accessible, collective activity capable of being pursued by suitably trained but relatively inexperienced chemists.

These papers show that Liebig's early students played an active part in establishing the Giessen research school and in the development of the new method of organic analysis using the *Kaliapparat*.[148] The *Kaliapparat* was not simply a necessary precursor to the creation of the research school, nor did it immediately reduce the practice of quantitative organic analysis to a routine task. Although Liebig produced the *Kaliapparat* as a means of overcoming problems in his own *research* into the composition of the alkaloids, establishing a stable investigative method based on this new piece of apparatus was achieved within the *pedagogical* context in the early Giessen research school. Liebig certainly sought to increase the research productivity of his Giessen laboratory by teaching his students to analyse organic substances and, notwithstanding the ability of Buff, Kodweiss and Oppermann to produce publishable analyses using the earlier method, the method of organic analysis using the *Kaliapparat* was essential in realising this goal.

Liebig's objectives in founding the Giessen research school were, however, not restricted to merely amplifying the ability of those in his own laboratory to tackle problems in organic analysis. The quality of his students' published work demonstrated the efficacy of Liebig's pedagogical approach and helped to establish the method of analysis using the *Kaliapparat* as trustworthy throughout the wider chemical community. The provision of a standardised, reliable and teachable

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[148] See also Jackson 2008.

method of quantitative organic analysis was an important goal for Liebig because he believed that organic chemistry could otherwise make little progress. The "old withering organic chemistry" of qualitative investigation must, in Liebig's view, give way to "the single and true way, the way of elementary analysis".[149] Whereas analysis was "the end goal" of inorganic investigations, in organic chemistry it was "the one safe reagent". As Liebig explained, "The mere description of the changes which an organic substance undergoes through the influence of other agents is truly hopeless, for it explains nothing if its composition is unknown to us".[150] And that had been the sticking point. Prior to the new method of analysis using the *Kaliapparat*, the composition of even relatively simple substances such as uric acid (*Harnsäure*) had remained impossible to establish because "none of the known analyses agrees with the others".[151]

The combined success of the analytical method using the *Kaliapparat* and the Giessen research school enabled Liebig to exert powerful control over the direction of research in organic chemistry and physiology.[152] Liebig's emphasis on the essential role of quantitative organic analysis in understanding chemical transformations, including those occurring in organic nature, owed quite a lot to his teachers Gay-Lussac and Thenard but his approach to prosecuting such investigations on a large scale and without the benefit of substantial financial support was entirely novel.[153] Liebig condemned Dumas' efforts to build a research group supported by personal patronage because "the times when Berthollet could gather a circle of eminently-talented young men around him at Arcueil are past".[154] Partly because of his limited resources, but also because stabilising his new method of analysis required the execution of very large numbers of analyses, Liebig created a new, professional approach to group research. The economy of work in the Giessen laboratory was a pragmatic response to local circumstances and the means by which Liebig advanced his own career, but it also represented Liebig's vision for the future of organic chemistry.[155] Piecing together the chain of knowledge of

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[149] Liebig 1834d, 173.
[150] Liebig (1834d, 173-174) compared the analytical approaches adopted by Büchner and Liebig's former pupil, Théophile-Jules Pelouze.
[151] Liebig 1834a, 47.
[152] On physiology, see Holmes 1964, vii.
[153] Gay-Lussac and Thenard 1811, 350.
*c.f.* for example, Liebig 1834g.
[154] Liebig 1832, 20. Cited in Partington 1964, 299. Rocke (2001, 115) explained that Dumas charged no fees to students in his private laboratory. On Dumas' research school see also Klostermann 1985.
[155] For more on the economy of work in the Giessen laboratory, see Jackson 2008.

organic substances "of which until now we can only follow a small stretch here and there" required a far greater number of chemists than could be provided by existing systems of training.[156] Liebig's Giessen research school produced dozens of young chemists skilled in organic analysis, including but by no means restricted to the use of the *Kaliapparat*, and I contend that in doing so it struck a fatal blow to the influence of Parisian chemistry and began the rise to dominance of German organic chemistry.

## Conclusion

This chapter has highlighted the extent to which work – rather than talent, good fortune or inspiration – was central to Liebig's achievements, whether in pursuit of his personal research goals or in the establishment of his research school. Individual success, though undoubtedly very important, was by no means sufficient to promote his vision for the future of organic chemistry as a discipline, with the result that Liebig devoted very considerable effort to his pedagogical project. Well before the introduction of the *Kaliapparat*, Liebig began training his students and assistants to make valuable and public contributions to the research output of his Giessen laboratory. Although the *Kaliapparat* failed to solve fully the tricky research problem of alkaloid analysis for which it was created, Liebig – assisted by his students and assistants – developed its use for non-nitrogenous substances into a pedagogically stable analytical method for the collective production of new knowledge. Liebig's success in creating a research school in Giessen therefore depended on his recognition of the practice of organic analysis as essentially communal – on his ability to mobilise the labour of young chemists within his laboratory and the promotional skill by which he gained acceptance for the new analytical practice throughout the wider chemical community – just as much as on his invention of the *Kaliapparat*.

Recognizing the novel economy of work in Giessen helps us to understand why Dumas was unsuccessful in maintaining, much less raising, the status of French chemistry during the 1830s and 40s, when Liebig's research school was reaching the peak of its international importance. In 1832, for example, whilst Liebig was struggling to build up the Giessen school, Dumas was able almost immediately to create a small research group by drawing on his private means. Whereas Liebig was forced by the limitations of his personal circumstances and position in Giessen to innovate, Dumas' private financial resources allowed him to preserve a more old-

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[156] Liebig 1834g, 2.

fashioned laboratory economy based on personal patronage. This approach to group research was certainly easier at the outset, but it ultimately proved unsuited to the new organic chemistry, whose emerging large-scale, professional nature was perceived and fostered by Liebig in his Giessen laboratory from the early 1830s.

Liebig appreciated the enormous importance of training in this new world, and that a school could exert a decisive influence on its students and on the progress of the discipline more generally. In 1834, for example, he published a brutal criticism of a paper by Pelletier – who had previously acted as mentor to the young Dumas – with the young chemist J. P. Couerbe. According to Liebig, their investigation of picrotoxin had produced a formula which "fits the analysis like the fist fits an eye".[157] Only at the very end of his remarks did a more sympathetic Liebig comment, "I consider it most deplorable that Hr. Couerbe, a young man of ability and great zeal, has entered a school which is so disadvantageous for him".[158] Seen in the context of his recent attempt to persuade chemists that properly executed analytical investigations were essential to the future of organic chemistry, Liebig's comments show that he not only deeply regretted the effect of poor training on individuals like Couerbe but was also aware that the discipline could not afford the misuse of their talents.

My revision of the origins and early development of the Giessen research school also has important implications for our understanding of the *Kaliapparat*. Whereas the new apparatus for organic analysis has previously been viewed predominantly within its pedagogical setting, I have claimed that it was originally the product of a highly competitive *research* context.[159] Improved alkaloid analyses were Liebig's weapon of choice in his attack on Dumas' superiority in the field of organic analysis, and the *Kaliapparat* provided him with an early, decisive success. Nevertheless, transforming quantitative organic analysis using the *Kaliapparat* from an instrument for personal research into a pedagogically stable *method* for collective investigation was demanding and time-consuming. The rapid expansion of the Giessen research school after 1835 certainly depended on the relative simplicity and reliability of organic analysis using the *Kaliapparat*, but these qualities were not automatically intrinsic to the piece of apparatus from the start. On the contrary, they were created by the painstaking integration of the *Kaliapparat* into a broader experimental system.

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[157] Liebig (1834b, 207) referring to Pelletier and Couerbe (1834).
[158] Liebig 1834b, 210.
[159] Usselman *et al.* (2005, 4) is unusual in considering Liebig's alkaloid analyses to be the principal motivation for his creation of the *Kaliapparat*.

What has so often been viewed in hindsight as a great man's inevitable rise to fame turns out to have been fraught with difficulty, and prosecuted at significant personal cost. Liebig later expressed the view that "talent really is will and work", and I have shown that Liebig expended plenty of both in becoming the acknowledged master of organic analysis and head of the famous Giessen school.[160]

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[160] Brown 1914a, 35. This was Campbell Brown's translation of Liebig's 1871 recollections.

# Chapter Two: Making Substances Speak

*Accurate chemical analysis is half an art, half a science.*

*Berzelius (1815).*[161]

## Introduction

Despite its importance in histories of nineteenth-century chemistry, we have until recently had only the most limited accounts of why and how Liebig's new apparatus for organic analysis – the *Kaliapparat* – was created, and what effect it had on the practice of organic analysis. To some extent, this can be attributed to the paucity of sources relating directly to these questions, so that any account necessarily relies on largely circumstantial evidence. The first such historical interpretation was published in 2005, when Melvyn Usselman, Alan Rocke, and their co-authors used Liebig's 1830 laboratory notebook together with correspondence between Liebig and Wöhler to present a "hypothetical route to the kaliapparat".[162] Their account, however, remained equivocal on some significant points, including the rapidity with which Liebig produced the first *Kaliapparat* and used it to obtain satisfactory analytical results, and the extent to which the new apparatus solved the problem of analysing the alkaloids. Instead, the main focus of their study, which included modern re-constructions of analysis using the *Kaliapparat*, concerned how easily the use of the new piece of apparatus – once developed – could travel, and the role of Liebig's 1837 *Introduction to the Analysis of Organic Bodies* in such transfer.

In this chapter, I use a more detailed analysis of Liebig's 1830 laboratory notebook to argue that the development of the *Kaliapparat* was rather more time-consuming than Usselman *et al.* suggested, and to show that analysing alkaloids such as morphine remained difficult even *with* the new piece of apparatus. Holmes warned that "research notebooks are not transparent accounts of the progress of an investigator along the historical trajectory leading to a discovery or other significant conclusion", and the "rather unsystematic" contents of Liebig's notebooks are no exception.[163] Despite this, Liebig's 1830 notebook allows us to "probe ... behind the public arenas of science to the semiprivate worlds in which individual investigators, or investigative groups, confront most directly the objects of their study", in this case Liebig's attempts to analyse various alkaloids including morphine.[164] Reading this notebook in the context of Liebig's published work and his correspondence with

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[161] Berzelius 1815a, 129.
[162] Usselman *et al.* 2005, 7-12; especially p. 7 on the paucity of published evidence.
[163] Holmes 2003, 297 ("research notebooks"); Holmes 1987a, 132 ("rather unsystematic").
[164] Holmes 1987a, 132.

other chemists provides detailed support for two major claims made in Chapter One. The first is that developing the method of organic analysis using the *Kaliapparat* took a lot of work; the second that the introduction of the *Kaliapparat* did *not* solve the problem of alkaloid analysis for which Liebig originally created it.

By comparing the results in Liebig's 1830 notebook with those he published for morphine in January 1831 I show that Liebig discarded many of his early analytical results, publishing only a limited selection of the experimental data he obtained. Even then, only *some* of these published results were used by Liebig to justify the formula – and particularly the nitrogen content – he proposed for morphine.[165] Although the *Kaliapparat* speeded up combustion analysis for a practised analyst, its application to analytical problems did not involve merely being able to use the apparatus correctly – what Faraday termed "mere manipulation".[166] Producing useful analytical results also required the analyst to select and interpret experimental results according to both empirical and theoretical criteria.

Similar claims concerning the role of judgement in Giessen laboratory practice emerged from Usselman *et al.*'s reconstructions of Liebig's first published analyses using the *Kaliapparat*.[167] Usselman, Rocke, and their co-authors asserted that "analyses *could* be judged by nineteenth-century chemists as good, by their obtaining replicated analyses with acceptable error limits".[168] They also found that the use of the *Kaliapparat* provided various forms of "visual feedback", according to which they were able to decide which analyses were reliable and which were likely to be faulty.[169] I showed in the previous chapter that two of Liebig's students, Blanchet and Sell, practised and published their method of achieving what Usselman *et al.* termed "replicative consistency", and in this chapter I argue that the exercise of judgement based on the analyst's sensory experience was an essential research skill taught in Liebig's Giessen laboratory.[170]

The use of skill and judgement in arbitrating between experimental data has preoccupied historians and philosophers of science for several generations. Are

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[165] Liebig's selection from amongst his published data has been noted but not explained by Usselman *et al.* (2005, 82).
[166] Faraday 1827, iii.
[167] Liebig's paper introducing the *Kaliapparat* (1831b) included analyses of a number of substances whose composition was well known, as well as of six alkaloids including morphine.
[168] Usselman *et al.* 2005, 14. Italics in original.
[169] Ibid., 24. Some of these forms of feedback were documented in Liebig 1837b.
[170] Ibid., 28. Achieving "replicative consistency" depended on obtaining consistent weights of carbon dioxide and water from all analyses of the same substance.

scientists justified in neglecting some of their results and, if so, how are we to understand the criteria they use in making such decisions? Two major studies have explicitly addressed these questions: Gerald Holton's detailed exposition of Robert Millikan's laboratory notes and publications in his work on the Millikan-Ehrenhaft controversy concerning the charge of the electron; and John Earman and Clark Glymour's investigation of Arthur Eddington's selective use of observations made during the 1919 solar eclipse to support Albert Einstein's general theory of relativity. Holton revealed that Millikan exercised various forms of judgement in his experimental work, but he reached no definite conclusion about their status within scientific practice.[171] For Earman and Glymour, meanwhile, Eddington's behaviour was perturbing because it threatened their belief in science as an objective, rational enterprise.[172] I argue that Liebig's approach to research, as exemplified by the work of his research group and explicitly documented in his publications, sheds considerable light on these issues, offering a unique insight into early nineteenth-century chemistry at the cutting edge. Research in Giessen incorporated analysis using the *Kaliapparat* as an integral component of an extended philosophy of practice in which the skilful exercise of judgement was both essential and teachable.

This understanding of the use of the *Kaliapparat* as merely one component in a broader experimental practice helps to explain a long-standing paradox. The introduction of the *Kaliapparat* has in retrospect come to be viewed as a crucial moment in the history of organic analysis, yet it excited relatively little comment at the time. Liebig was successful in that his new apparatus was adopted for the determination of carbon during the following year or two by many of his peers, including both Wöhler and Dumas. But his 1830 alkaloid analyses – though they provided useful support for the idea that the basicity of the alkaloids was directly related to their nitrogen content – did not produce formulae which were instantaneously and universally accepted.[173] Moreover, as I show here, chemists including Dumas did not apply the *Kaliapparat* to what Liebig regarded as its most important purpose in the context of research: acting as a control on the analysis of *nitrogen*.[174]

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[171] Holton 1978a, 52-54 and 71-72.
[172] Earman and Glymour 1980, 85.
[173] See, for example, Dumas 1830; and Regnault 1838.
[174] Wöhler to Berzelius, 24 November 1831, in Wallach (1901, 380-381) described how Wöhler learnt to use the *Kaliapparat* in Giessen in late 1831. The following year, Wöhler and Liebig (1832) published their (truly) joint investigation of the benzoyl radical. Dumas (1834) adopted the *Kaliapparat* for the determination of carbon, but did *not* use it to provide a control on the determination of nitrogen.

I argue that Liebig's analytical practice as a whole was much harder to establish in Giessen, and proved considerably more contentious and difficult to propagate in the chemical community elsewhere, than has previously been acknowledged. In relation to the determination of nitrogen, Liebig ultimately failed to establish the superiority of his analytical approach. Several years' hard work by Liebig, together with his students and assistants, enabled the development of what I shall call the *Giessen approach to organic analysis* but, as I mentioned in Chapter One, this did not include the analysis of nitrogenous substances. Liebig himself continued to analyse nitrogen-containing compounds, including uric and hippuric acids, but even the impassioned plea with which he opened his 1834 paper *On some Nitrogen Compounds* did not succeed in establishing the role of the *Kaliapparat* in the determination of nitrogen.[175] Partly as a consequence of this failure, I contend that one of Liebig's major goals from the late-1830s was to establish the Giessen approach to the analysis of non-nitrogenous organic substances as standard practice across Europe.[176]

In this context, moreover, his 1837 *Introduction to the Analysis of Organic Bodies*, which has usually been seen as simply a textbook manifestation of the 1831 method of analysis using the *Kaliapparat*, emerges as an important means by which Liebig sought converts to his methods. I showed in the previous chapter that Liebig used papers he and his students published in the *Annalen der Pharmacie* to advertise and build trust in his analytical approach. Liebig also used his role as editor of the *Annalen* to promote and defend the research output of his laboratory and to criticise analytical work he regarded as deficient. Liebig's exchanges with other chemists in the pages of the *Annalen* were frequently heated and I argue in the final section of this chapter that this vehemence was at least partly a consequence of his growing frustration at the persistent failure of these chemists to adopt the Giessen approach to organic analysis in its entirety.

I have already referred at various points in this dissertation to the problem of alkaloid analysis, and the difficulties of organic analysis more generally. I therefore begin by going back, if not quite to the beginning, then at least far enough to show clearly what problems confronted chemists as they attempted to discover the elemental

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[175] Liebig 1834a for uric acid; 1834e and 1834f for hippuric acid; and 1834g on nitrogenous substances.

[176] Rocke (2001, 53-55) has discussed Dumas' (1833) introduction of a new method for determination of nitrogen which became accepted as the "best general method of its type". Liebig (1837b) included this method but did not mention the use of the *Kaliapparat* as a control for nitrogen determination.

composition of purified organic substances in the early decades of the nineteenth century. The following section, like the chapter as a whole, necessarily contains some moderately technical discussion of various methods of quantitative organic analysis, including their experimental execution as well as the numerical treatment of the raw results they produced. I have, however, kept such discussion to the minimum necessary to support my arguments, and tried to be as consistent as possible in using technical terms – all of which are explained on first use, along with contemporary synonyms and (rough) modern equivalents, in either in the main body of the text or in the numbered footnotes.

## The Problem of Organic Analysis

> *It is only within the last thirty years that this department of chemistry [the analysis of organic substances] has been cultivated on scientific principles; and all the lately proposed methods differ from one another only in the way in which those principles are carried out*
>
> *Justus Liebig (1837)*[177]

The principle of quantitative organic analysis is the determination of the percentage by mass of the elements of which a pure organic compound is composed, called its *composition*.[178] Finding the composition of an organic substance and converting this composition into a *formula*, first *empirical* and then *molecular*, has now been a rather routine aspect of the practice of organic chemistry for almost 150 years.[179] This familiarity, combined with the conceptual simplicity of the process, has led most historians of chemistry to overlook the constructed nature of such apparently fundamental notions as *pure organic compound* and *formula*. Despite the important work done by Ursula Klein and Wolfgang Lefèvre in drawing attention to the need to historicise ideas like *purity* and *formula*, the history of organic analysis continues to be rather neglected by historians except in so far as it relates to theoretical debates about the *constitution* of (or arrangement of the elements within) organic compounds during the 1830s and 40s.[180] In fact, the *practice* of organic analysis was a good deal more difficult than is usually acknowledged by such histories, and

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[177] Liebig (1837b 1) translated by William Gregory in Liebig (1839b, 1).
[178] What I refer to as quantitative organic analysis is often referred to as elemental (in relation to Lavoisierian elements) or ultimate (as a means of distinguishing it from earlier traditions of proximate analysis).
[179] The empirical formula shows the ratio of number of atoms of each kind in a substance, whilst the molecular formula shows the number of atoms of each kind in one molecule.
[180] On the historicity of purity, see Klein and Lefèvre 2007. Klein (2003) studied of the role of constitutional theories in the construction of Berzelian formulae, and the power of those formulae in producing knowledge about chemical transformations. The standard history of chemical analysis is Szabadváry 1992. Holmes (1963) did not aim to provide comprehensive coverage of its apparatus and methods, but presented a much clearer historiography of the development of organic analysis between about 1780 and 1840.

understanding why that was so and how chemists overcame those difficulties helps to explain the changing meaning of terms like purity, identity and formula during the nineteenth century.

For one thing, what were considered during the late-eighteenth and early nineteenth centuries to be single organic substances often produced widely differing analytical results, which in turn implied that the composition of such substances might be variable. Chemists' understanding of these observations began to change as they developed new techniques of purification and proximate analysis around 1800.[181] During the early-nineteenth century, partly as a result of the development of quantitative organic analysis, chemists began to re-conceptualise plant materials as "purified carbon compounds" of fixed composition with the result that many organic substances came to be regarded as complex mixtures of organic compounds whose composition, like those of inorganic substances, was fixed.[182] Compared with the analysis of inorganic substances, which by this time used established experimental methods to place a substance within a well ordered and fairly stable taxonomy, quantitative organic analysis remained problematic in practical as well as theoretical terms.[183]

The question of purity was of particular significance in the analysis of organic compounds. Whereas inorganic substances usually contain two or three from a wide variety of possible elements, most organic compounds are formed from carbon plus one or more of the three elements: hydrogen, oxygen and nitrogen. So whilst the diversity of inorganic substances derives to a large extent from *which* elements they contain, the existence of an extremely large number of organic compounds is partly the result of the combination of the same few elements in extraordinarily varied proportions.[184] *Composition*, expressed as percentages by mass of carbon, hydrogen, oxygen and (sometimes) nitrogen, was therefore extremely similar for a large number of substances whose chemical properties were quite different. In these circumstances, and particularly following the introduction of Berzelian formulae, the *accuracy* of quantitative organic analysis became a dominant concern, since this was the only way to preserve chemists' theory that distinct substances should have different composition. Separating a single, pure organic compound

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[181] Holmes 1971. Proximate (as opposed to ultimate) analysis referred to the separation of a substance into components which were not elementary.
[182] Klein 2005, 261.
[183] See Klein and Lefèvre (2007, Chapter 3) on the importance of classification in eighteenth-century chemistry.
[184] See Berzelius (1814a, 1814b, 1815b, 1815c, 1815d) on the complex composition of organic bodies and the consequent difficulty of their analysis.

from the other, often very similar compounds with which it occurred in nature, became an essential first step in reliable quantitative organic analysis.

New techniques of purification revealed the complexity of natural organic materials, but it frequently remained impossible to prepare their constituent substances in sufficient purity for meaningful quantitative analysis. Even where a relatively pure compound could be obtained and its composition determined, interpreting that data was far from easy. By the early 1830s, for example, many quite different organic substances were known to share the same composition, a phenomenon chemists struggled to reconcile with their existing theoretical beliefs. Theories of chemical constitution incorporating ideas about the assembly of elements within organic substances were introduced in response to this problem, but there was little agreement about the validity of such theories and no concept equivalent to the modern idea of chemical structure at this time. As Liebig explained in 1834, "One has known the percentage composition of ether, spirit of wine and their compounds with certainty for a long time, but one has only more or less probable suppositions concerning the manner in which their elements are joined together".[185]

The first quantitative analyses of organic substances were attempted by Antoine Lavoisier in the 1780s, when he burnt substances including alcohol and organic oils in oxygen gas and collected the water and carbon dioxide produced.[186] Lavoisier confirmed that organic substances contained the elements carbon and hydrogen but his analyses failed to produce reliable quantitative data, despite the extreme care and ingenuity lavished by instrument makers including Nicolas Fortin on the construction of his apparatus. As a result, Lavoisier's contribution in this area has often been considered to be restricted to the *principle* that the quantities of carbon and hydrogen in organic bodies could be determined by burning the substance completely and collecting the water and carbon dioxide so produced.[187] I contend that this underestimates the contemporary value and historical interest of Lavoisier's analytical technique. In line with his broad commitment to experimental approaches based on gravimetric measurement, Lavoisier's method of organic analysis involved gravimetric determinations of both hydrogen and carbon. Steam produced by combustion was condensed to water, which was collected and weighed, whilst carbon dioxide gas was trapped using a piece of apparatus remarkably reminiscent of the *Kaliapparat* introduced by Liebig over forty years later (Figure 2). The gas

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[185] Liebig 1834c, 321.
[186] Lavoisier 1784.
[187] See, for example, Szabadváry 1992, 285.

passed through a series of up to nine glass bulbs connected by brass tubing, each about half full of sodium hydroxide solution. Acidic carbon dioxide dissolved in the alkaline solution, several bulbs being used in sequence to ensure that none of the gas escaped, so that the increase in mass of the bulbs would give a direct measure of the mass of carbon dioxide produced.[188]

Lavoisier's followers Joseph-Louis Gay-Lussac and Louis-Jacques Thenard continued his programme of organic analysis, seeking the quantitative accuracy which had eluded Lavoisier. They adapted the analytical procedure to use volumetric methods, which made use of their considerable experimental expertise in the accurate measurement of gas volumes and which they considered far more accurate than the gravimetric approach used by Lavoisier.[189] Gay-Lussac and Thenard believed that the lack of accurate analytical data had been largely responsible for limited progress in plant and animal chemistry during recent years. Their new method of analysis relied on a rather complicated apparatus (Figure 3) and involved the combustion of pellets of organic substance mixed with potassium chlorate, introduced here as an alternative source of oxygen to ensure complete combustion. They reported the analyses of a number of organic substances including several organic acids, using these results to propose a general relationship between the relative proportions of hydrogen and oxygen and the acid-base behaviour of the substance. By 1816, Thenard had abandoned that interpretation of their results, but he continued to defend the superior accuracy of their volumetric approach when compared with other methods in use at the time.[190] As late as 1828, Gay-Lussac was adamant that: "In the analysis of plants, it is necessary to try to obtain gaseous products rather than solid products, because with gaseous products, one attains a greater degree of precision."[191]

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[188] Lavoisier (1864, 347-351). Note that this apparatus is not the one used in Lavoisier's published analyses, cited above. I infer, however, from his description of an analysis of sugar in Lavoisier (1865, 774) that Lavoisier used this apparatus during 1788.
[189] Gay-Lussac and Thenard 1811, 267-8.
[190] Thenard (1816, 192-205) contained a detailed critique of the methods used by Berzelius and the Swiss analyst Théodore de Saussure.
[191] Gay-Lussac 1828, 26. Crosland (1978, 110-113) discussed the influence of Gay-Lussac's volumetric approach on the work of other scientists, including Berzelius, Dumas and Liebig, on the determination of atomic weights. Liebig, like Berzelius, eventually reverted to gravimetric methods.

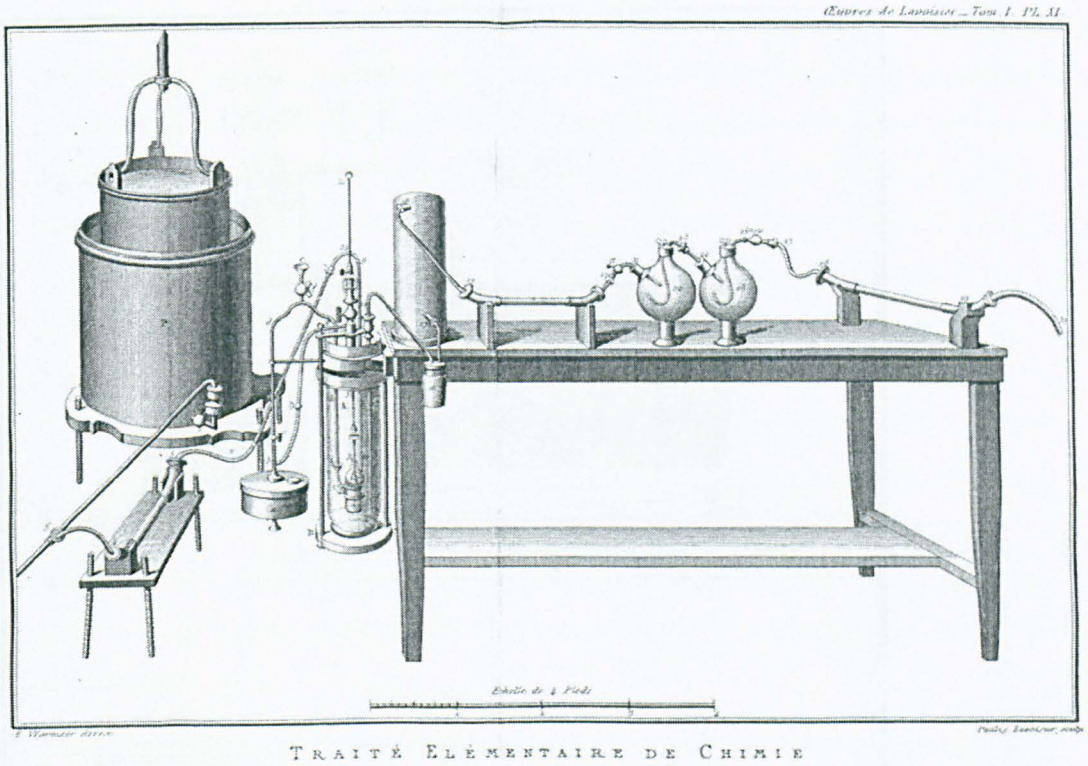


Figure 2. Lavoisier (1864, 347-351) described this apparatus for organic analysis (illustrated Plate XI) and its use in the combustion of oils. Although the illustration shows only two glass bulbs, Lavoisier (1865, 774) referred to his use of up to *nine* bulbs, connected by brass tubing and part-filled with sodium hydroxide solution, in attempting to ensure complete absorption of the carbon dioxide produced on combustion of sugar. A similar apparatus including five glass bulbs – attributed to the celebrated Parisian instrument maker Nicolas Fortin - is displayed in the Conservatoire National des Arts et Métiers, Paris.

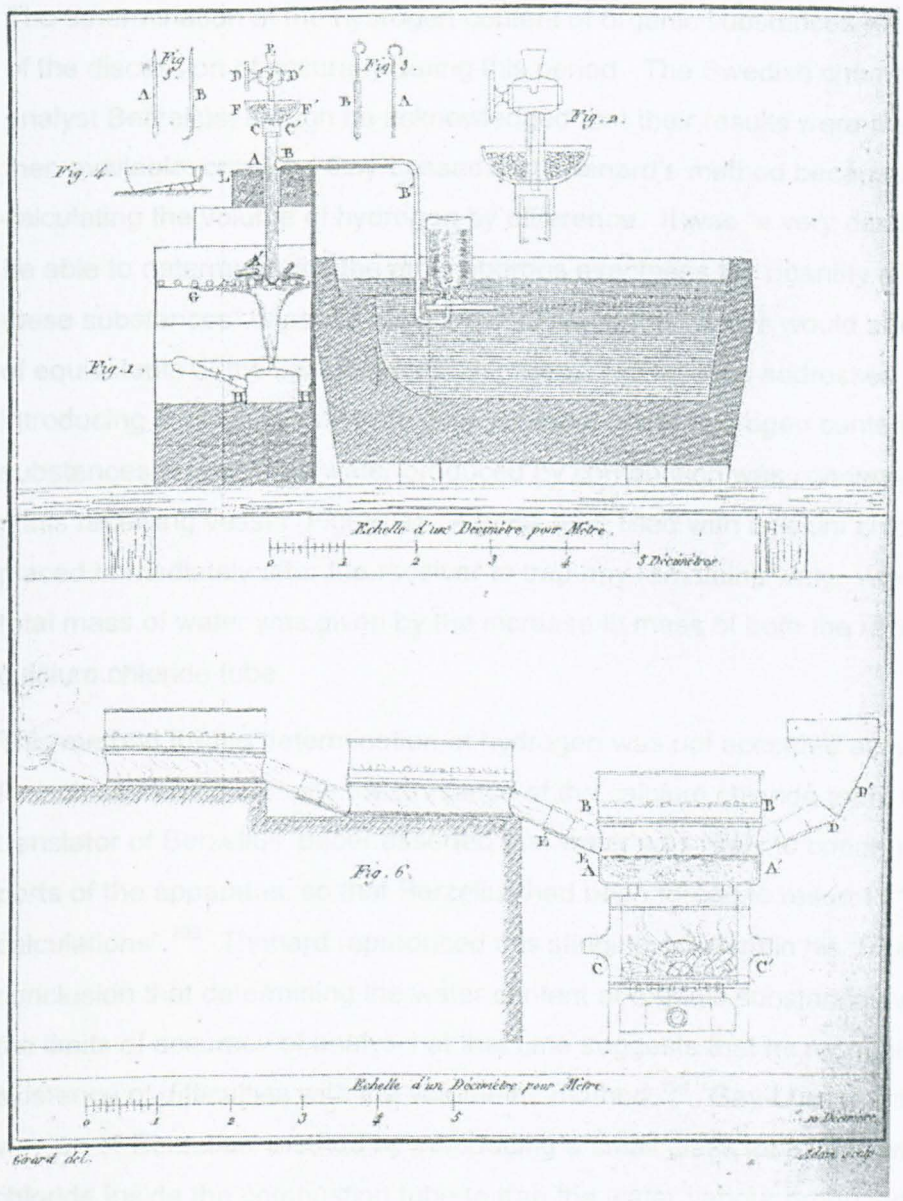


Figure 3. Gay-Lussac and Thenard's (1811, Plate 6) apparatus for organic analysis incorporated a vertical combustion tube fitted with a special air tight tap, and relied on volumetric measurement of the gas produced.

The determination of the hydrogen content of organic substances was a major focus of the discussion of accuracy during this period. The Swedish chemist and master analyst Berzelius, though he acknowledged that their results were the most accurate then available, criticised Gay-Lussac and Thenard's method because it relied on calculating the volume of hydrogen by difference. It was "a very essential point to be able to determine with the most rigorous exactness the quantity of hydrogen in these substances" because even small experimental errors would affect the number of equivalents of the light element hydrogen.[192] Berzelius addressed this issue by introducing a direct, gravimetric determination of the hydrogen content of organic substances in which the water produced by combustion was condensed in a small, glass receiving vessel (Figure 4). A glass tube filled with calcium chloride was placed immediately after the receiver to trap any remaining water vapour, and the total mass of water was given by the increase in mass of both the receiver and the calcium chloride tube.

This method for the determination of hydrogen was not accepted as superior by French chemists. Despite the presence of the calcium chloride tube, the French translator of Berzelius' paper asserted that water was likely to condense in other parts of the apparatus, so that Berzelius had been forced to resort to "hypothetical calculations".[193] Thenard reproduced this stinging criticism in his *Traité*, but his conclusion that determining the water content of organic substances was beyond the limits of accuracy of analysis at that time suggests that he recognised the existence of difficulties with the volumetric method.[194] Gay-Lussac adapted a version of Berzelius' method by introducing a small glass tube filled with calcium chloride inside the combustion tube to trap the water vapour produced by combustion, so that no water vapour was collected with the other gases for volumetric analysis.[195] Other practitioners used variations on these methods, but by the late 1820s most chemists used a glass U-tube filled with calcium chloride to trap

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[192] Berzelius 1814b, 402.
[193] Thenard 1816, 200-201.
[194] Ibid., 202.
[195] Gay-Lussac 1815a and 1815b.

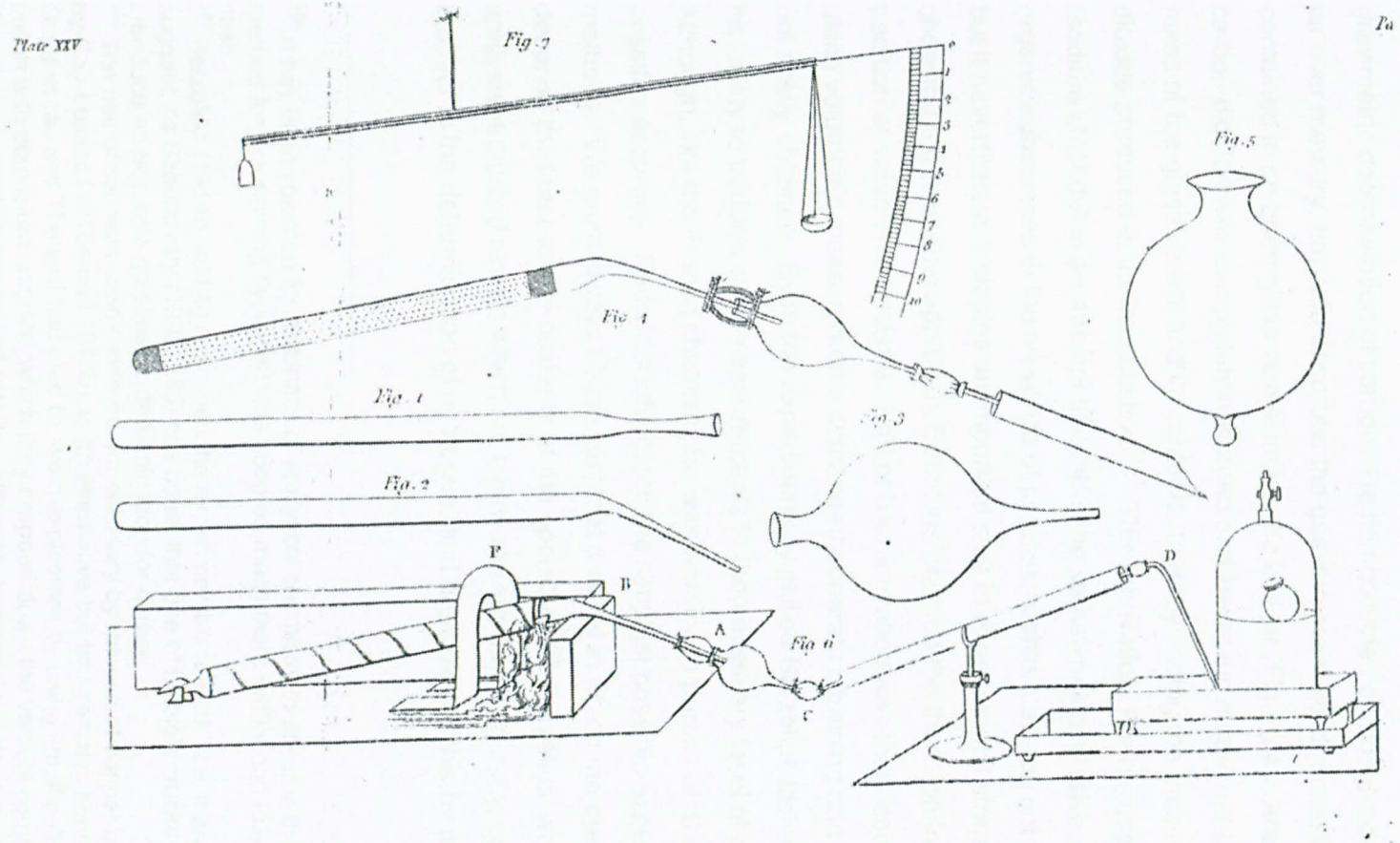


Figure 4. Berzelius (1814b) produced his apparatus for organic analysis by glassblowing. The combustion tube was horizontal, and both water and carbon dioxide were determined gravimetrically. Water was trapped in a small condenser (shown life-size in *Fig. 3*) followed by a tube containing calcium chloride. Carbon dioxide gas was collected over mercury before being absorbed in a glass vessel (shown life-size in *Fig. 5*) containing solid potassium hydroxide.

water vapour as it emerged from the combustion tube, so that a direct, gravimetric determination of hydrogen based loosely on Berzelius' method became the standard.[196]

As well as arranging the combustion tube horizontally, Berzelius also reverted to a gravimetric determination of carbon. He first collected carbon dioxide gas in a bell jar over mercury, but then absorbed the gas into moist solid potassium hydroxide contained in an open glass vessel inside the bell jar (Figure 4). After 24 hours, the carbon dioxide was completely absorbed and Berzelius measured the increase in mass of the glass vessel and its contents, thereby finding the mass of carbon dioxide produced in the combustion.[197] This innovation, like his use of common salt (sodium chloride) in an attempt to control the sometimes explosive combustion of organic substances in the presence of potassium chlorate, was not widely adopted but it nevertheless indicates an important shift in experimental strategy.[198] By choosing a gravimetric approach, Berzelius rejected the then dominant French tradition of volumetric analysis. Part of his motivation was that accurate analysis using volumetric measurements demanded apparatus, training and skill that were not easily obtained. Even the experimentally skilled Berzelius lacked confidence in his ability to perform such measurements to the necessary level of accuracy.[199] Although, like the French chemists, he was working in pursuit of "the utmost possible accuracy", Berzelius advocated the simplest possible experimental methods: "We must always chuse [sic] that method in which the precision of result depends the least on the dexterity of the operator".[200] Berzelius' work in organic analysis produced results which set a new standard for accuracy, particularly with respect to the determination of hydrogen, and he achieved this by making more

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[196] It has been common for historians of analytical chemistry to assume that Berzelius' method for determining hydrogen was adopted much more swiftly and fully than was the case.

[197] Berzelius (1814b, 404-6) described the experimental method. It is therefore incorrect to suggest, as Szabadváry (1992, 285) has done, that one of Liebig's crucial innovations was to introduce an accurate gravimetric determination for carbon.

[198] The use of salt was soon rendered unnecessary by the use of copper oxide, introduced by Gay-Lussac (1815a and 1815b) as an alternative but less reactive source of oxygen. Gay-Lussac and Thenard had tried to avoid explosions by using small pellets of sample mixed with potassium chlorate, which they dropped down the vertical combustion tube. Berzelius' innovation had mixed results. Although it reduced the danger of carrying out combustions, the presence of salt led to the formation of organic chlorides, which very significantly complicated the processing of results obtained using Berzelius' method. See Thenard 1816, 195.

[199] Crosland (1967, 415) described Berzelius' decision to leave delicate volumetric measurements to Dulong during his visit to Paris in 1819.

[200] Berzelius 1815a, 129.

straightforward gravimetric measurements using apparatus he had constructed from relatively simple, cheap items of glass apparatus.

By the 1820s, when Liebig learnt organic analysis in Paris, the first outcome of quantitative organic analysis was a measured quantity of carbon dioxide and of water, produced by complete oxidation of the carbon and hydrogen contained in a sample of known mass. In Gay-Lussac's laboratory the mass of hydrogen was determined directly using a modification of Berzelius' gravimetric technique, but Liebig learnt Gay-Lussac's volumetric method for determining carbon (Figure 5). In this procedure, steam was removed from the exhaust gases by using a calcium chloride tube, the remaining gas being collected in a graduated jar over mercury. Provided that the sample was pure and contained no nitrogen (or other elements), then this gas was pure, dry carbon dioxide. Its volume was corrected to standard conditions of temperature and pressure and used to calculate the percentage mass of carbon. The percentage oxygen was found by difference, again provided that the substance contained no nitrogen (or other, more unusual element such as sulphur or phosphorus).

Following the introduction of Berzelian formulae, a further step involved providing a formula to fit this data, as exemplified in the series of organic analyses published by Berzelius in 1815.[201] It became usual practice to publish the theoretical composition based on this formula, in order to show how close the agreement with experiment was.[202] Largely because analytical data rarely enabled the unambiguous assignment of formula, chemists were at pains to demonstrate the accuracy of their results and hence justify their choice of formula.[203] In many cases, carbon content could be determined with sufficient accuracy to specify the number of equivalents of carbon unambiguously but, as Liebig realised during the late 1820s, this was not the case for substances of high molecular weight including the alkaloids. The existing volumetric method produced sufficiently accurate analytical data for relatively simple substances when performed by a skilled analyst, but many organic substances could not be analysed reliably in this way.

The determination of nitrogen was even more problematic, mainly because the strongly oxidising conditions used to ensure the complete conversion of carbon to

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[201] Berzelius 1815b, 1815c, 1815d.
[202] See, for example, Dumas and Pelletier 1823, 191.
[203] Klein (2003) has examined the role played by constitutional theory in directing chemists' selection of formula.

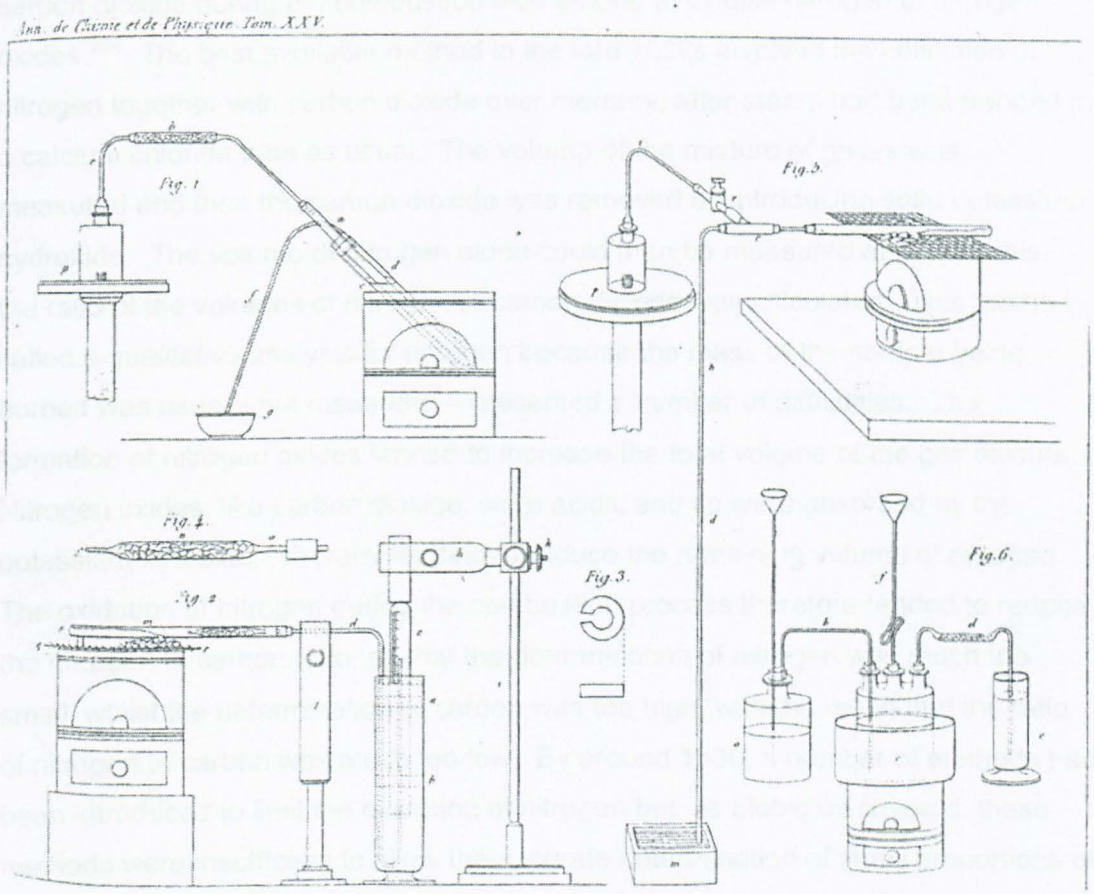


Figure 5. Liebig and Gay-Lussac (1824) illustrated the apparatus (*Fig.* 2) used by Liebig to carry out the analysis of silver fulminate. The horizontal combustion tube contained a small calcium chloride tube to trap water vapour, so that only carbon dioxide gas was collected for volumetric determination.

carbon dioxide during the combustion also tended to oxidise nitrogen to nitrogen oxides.[204] The best available method in the late 1820s involved the collection of nitrogen together with carbon dioxide over mercury, after steam had been trapped in a calcium chloride tube as usual. The volume of the mixture of gases was measured and then the carbon dioxide was removed by introducing solid potassium hydroxide. The volume of nitrogen alone could then be measured and, from this, the ratio of the volumes of nitrogen to carbon dioxide was calculated. This method – called a *qualitative* analysis for nitrogen because the mass of the sample being burned was usually not measured – presented a number of difficulties. The formation of nitrogen oxides tended to increase the total volume of the gas mixture. Nitrogen oxides, like carbon dioxide, were acidic and so were absorbed by the potassium hydroxide, thereby tending to reduce the remaining volume of nitrogen. The oxidation of nitrogen during the combustion process therefore tended to reduce the nitrogen to carbon ratio, so that the determination of nitrogen was much too small, whilst the determination of carbon was too high, with the result that the ratio of nitrogen to carbon was much too low. By around 1830, a number of methods had been introduced to limit the oxidation of nitrogen but, as Liebig discovered, these methods were insufficient to allow the accurate determination of small proportions of nitrogen, such as existed in the alkaloids.

At the time when Liebig began working in the field of organic analysis, therefore, he faced a number of technical obstacles mainly concerned with the determination of carbon and nitrogen in substances of high molecular weight. In tackling these problems Liebig developed the *Kaliapparat*, his new apparatus for determining carbon content by gravimetric measurement, but this was merely one aspect of his new analytical practice. The analysis of the alkaloids also involved finding their nitrogen content and, despite Liebig's best efforts, this remained highly problematic throughout the 1830s. Making sense of the analytical data produced by experiment was not straightforward, and Liebig introduced a complex series of procedures, data-selections and empirically determined corrections in order to produce reasonable formulae from highly indeterminate experimental data.

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[204] This had been a particular problem when using the powerful oxidant potassium chlorate, but continued to be problematic even after the introduction of copper oxide.

## The *Kaliapparat* and Liebig's Alkaloid Analyses

> *The small amount of the organic substance one is used to subjecting to analysis makes an exact determination of the carbon and nitrogen in bodies possessing as great an atomic weight as the salifiable vegetable bases quite impossible.*
>
> *Justus Liebig (1831)*[205]

I argued in Chapter One that the *Kaliapparat* was initially the product of a competitive research environment, and that its pedagogical significance developed between 1831 and 1834. This idea is supported by Liebig's first public presentation of his new apparatus for analysis (Figure 6), published in Poggendorff's *Annalen der Physik und Chemie* in January 1831. According to that paper, Liebig's primary motive for developing the *Kaliapparat* was to improve the accuracy and reliability of the determination of carbon.[206] Whereas an error of 1% in the carbon content generally did not affect the number of carbon atoms in an organic substance, in the case of the alkaloids an error of this magnitude was crucial.[207] Liebig had hoped to minimise this error by subjecting much larger samples to analysis, which he was able to do because his new apparatus trapped carbon dioxide in condensed form rather than as a gas,[208] but Liebig quite explicitly avoided claiming increased *accuracy* for analysis using the *Kaliapparat*. "Nothing is new about this apparatus", Liebig declared, "apart from its simplicity, and the complete reliability which it offers".[209] He described its form and function in some detail in this paper, but Liebig provided insufficient information in this paper to enable others to repeat his experimental work. In particular, although the *Kaliapparat* was illustrated, Liebig did not include any instructions for how this novel piece of glassware might be created.[210] Far from being a triumphant announcement that his new apparatus had solved the existing problems of organic analysis, Liebig's introduction of the *Kaliapparat* was rather modest and gave no particular indication that he expected

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[205] Liebig 1831b, 1.
[206] Ibid.
[207] Liebig himself used the term *atom*, though this was later largely replaced by *equivalent* in order to reflect chemists' growing ambivalence concerning the ontological status of atoms. Compare, for example, Liebig 1837b and 1853.
[208] Liebig's general approach here was *not* new. Gay-Lussac had already applied this strategy to the determination of hydrogen. By carrying out a separate combustion to determine hydrogen, in which water vapour was trapped by a calcium chloride tube and the other combustion products were released to the atmosphere as gases, Gay-Lussac removed the limitations on sample size caused by the collection of gaseous products.
[209] Liebig 1831b, 4-5.
[210] Liebig (1831b, 12-13) referred the reader in a footnote to Batka in Prague for the supply of the apparatus described, but it is far from clear that this included the *Kaliapparat*.

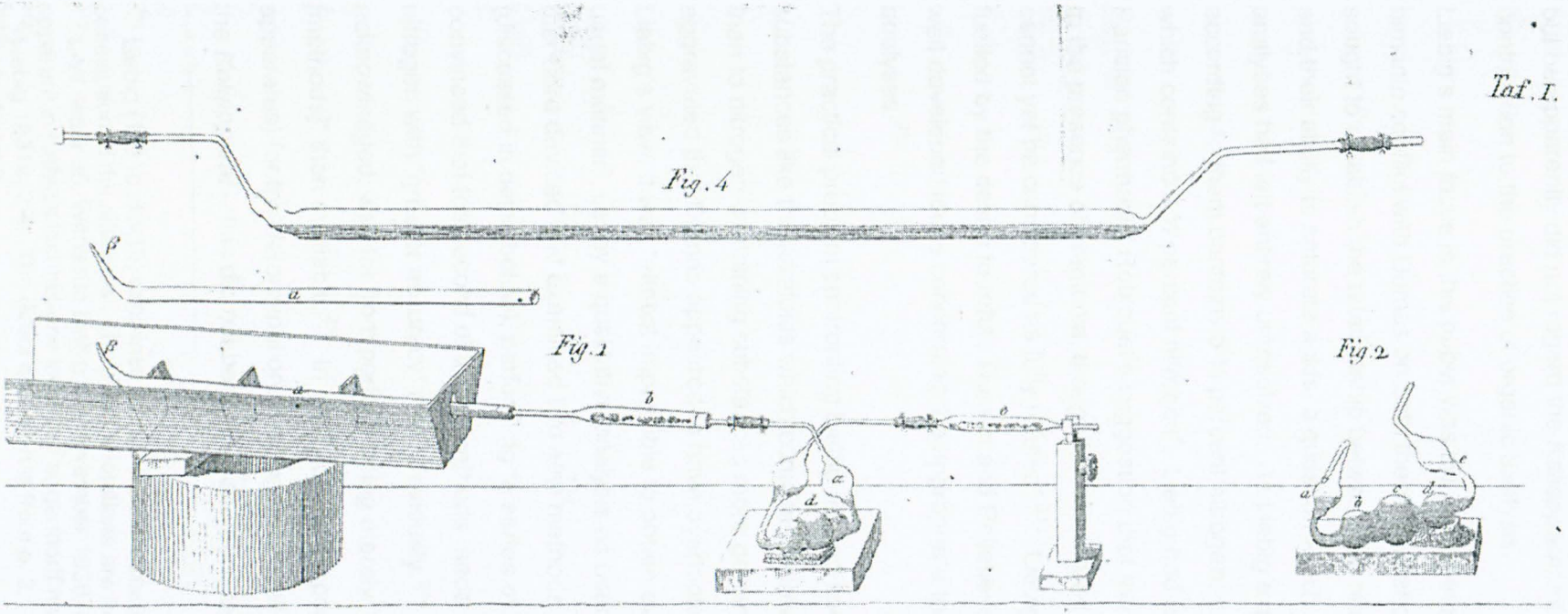


Figure 6. When Liebig (1831b) introduced the *Kaliapparat*, he illustrated its use but provided no instructions on how to make it.

others to adopt his new apparatus. After months of work, Liebig was able to report analyses he regarded as a significant improvement on those of Dumas and Pelletier, but he apparently did not regard the *Kaliapparat* as anything more than a useful contribution to the practice of organic analysis.

Liebig's main focus in this paper was the determination of nitrogen, which brought him into conflict with Dumas on both theoretical and practical grounds. Liebig sought to establish the relationship between the nitrogen content of the alkaloids and their ability to saturate acids, a question which Dumas and Pelletier's earlier analyses had left entirely unresolved. As Liebig explained, "morphine, which according to them contains 5 ¼ percent nitrogen, saturates more acid than quinine, which contains 8 ½ percent nitrogen". Liebig had also hoped to disprove the Parisian pharmacist Robiquet's suggestion that the basicity of the alkaloids was due to the presence of ammonia, though he was forced to concede that: "this opinion cannot yet be considered as fully refuted".[211] Liebig's "analysis mania" had been fuelled by the desire to refute Dumas and Pelletier's analyses, but he also had quite well developed ideas concerning the appropriate theoretical outcome of his alkaloid analyses.[212]

The practical problem confronting Liebig related specifically to the analysis of substances like the alkaloids which contained a low percentage of nitrogen, rather than to nitrogen-containing substances more generally, and he was clearly aggravated that Dumas appeared to have overlooked this important distinction. In Liebig's view, it was "almost impossible to obtain even approximate results in the usual manner", i.e. by a qualitative analysis as used by Dumas.[213] Liebig had therefore devised and examined two new methods for determining nitrogen (discussed in detail below), performing "a series of futile experiments" before he was convinced that the second of these methods made possible the determination of nitrogen with "greater accuracy" than previously.[214] His new method, Liebig acknowledged, was far from perfect, being merely "the least bad amongst the bad [methods]" then available.[215] In 1831, Liebig proposed a new method (and apparatus) for the determination of nitrogen as well as carbon but because – unlike the *Kaliapparat* – this did not become a standard technique of organic analysis it has

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[211] Liebig (1831b, 13-16) explained the theoretical debates surrounding the composition and constitution of the alkaloids. The direct quotations are from p. 14.
[212] L-W, letter 35, Wöhler to Liebig, 28 November 1830, described how the "Analysier-Manie" apparent in Liebig's last-but-one letter to Poggendorff had amused the Berlin chemists.
[213] Liebig 1831b, 2-4. The direct quotation is from p. 2.
[214] Ibid., 4 and 9.
[215] Ibid., 10.

been little remarked upon by historians.[216] In fact, a very large proportion of the vast effort Liebig expended on the analysis of the alkaloids was devoted to determining their nitrogen content with greater accuracy than had been achieved by Dumas and Pelletier in 1823.[217]

I mentioned in Chapter One that Liebig had been convinced by his 1829 analysis of morphine that existing methods of determining nitrogen were inadequate for the analysis of alkaloids, and that Dumas and Pelletier's earlier analyses were flawed.[218] He began to analyse nitrogen-containing organic substances during the early summer of 1830 and by August, Liebig was developing a new apparatus for nitrogen determination.[219] Well before he embarked on the series of alkaloid analyses which would occupy him from October to December, and whilst analysing substances with a relatively large nitrogen content, Liebig was already searching for an improvement to the existing qualitative method for nitrogen. A more viable method of nitrogen determination was, according to Liebig, urgently needed for organic analysis and he dismissed new apparatus, such as that introduced by William Prout in 1827, as redundant if it did not contribute to the solution of this problem.[220] Liebig learnt, moreover, that the accuracy with which nitrogen content could be determined using the method of qualitative analysis was necessarily connected to the accuracy of the carbon determination, and that this problem was particularly severe where the ratio of nitrogen to carbon fell below 1:5.[221] Liebig's original motivation for analysing the alkaloids was to dispute their nitrogen content as determined by Dumas and Pelletier, and I agree with Holmes that it was whilst addressing *this* problem that he realised it was *also* necessary to improve the accuracy and reliability of the determination of carbon.[222] As Liebig commented in his first letter to Berzelius in January 1831, he had felt "compelled" to invent a new

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[216] Even Holmes, though he noted (1973, 331-332) the difficulty nitrogen determination posed, did not provide an account of Liebig's contributions in this area.
[217] See, for example, Liebig (1831b, 18-19) for his refutation of the value obtained by Dumas and Pelletier for the nitrogen content of morphine.
[218] Dumas and Pelletier 1823 cf. Liebig 1829.
[219] L-W, letter 18, Liebig to Wöhler, 26 June 1830, shows that Liebig was analysing nitrogen containing substances. By letter 20, Liebig to Wöhler, [4] August 1830, Liebig was contemplating the analysis of alkaloids and planning a new apparatus for nitrogen determination. The first reference specifically to *alkaloid* analyses occurs in letter 29, Liebig to Wöhler, 12 October 1830, which tends to confirm the provisional date suggested by Usselman *et al.* (2005) for the start of this body of work.
[220] Prout 1827. Liebig (1830a, 357) claimed that Prout's method was much more complicated than others already in existence, and that his analyses had not changed the number of atoms of each kind in the substances he had analysed.
[221] Liebig (1831b, 8-9) explained this problem by using the example of morphine, for which the most accurately measured ratio of nitrogen to carbon was then 1:34.
[222] Holmes 1973, 331.

piece of apparatus in order to overcome some of the difficulties he experienced when attempting to analyse alkaloids using the existing experimental procedures.[223]

## The notebook

In what follows, I use Liebig's 1830 laboratory notebook as my main source for a reconstruction of his approach to the analysis of the alkaloids, including his development of the *Kaliapparat* and the methods he used to determine their nitrogen content. This notebook is one of a small number in the Liebigiana collection in the Bavarian State Library in Munich.[224] In 1987, Frederic Holmes suggested that the few surviving, "rather unsystematic notebooks" might not provide "sufficient detail and coverage to reconstruct an unbroken research trail" for Liebig, and this is perhaps partly why so little use has been made of these valuable sources during the past twenty years. Even when supplemented by Liebig's "intense" scientific correspondence, Holmes clearly doubted scholars' ability to overcome the barriers Liebig's notebooks raised to "penetration through the filters of his published research papers".[225] Indeed, the only use of this material so far has been in the work of Usselman *et al.* referred to earlier, where the 1830 notebook together with the correspondence between Liebig and Wöhler played a crucial role in their reconstruction of Liebig's invention of the *Kaliapparat*. Tackling Liebig's 1830 laboratory notebook was therefore a rather daunting prospect, and I was not encouraged to notice that in April 1831 Liebig was unable to follow his *own* laboratory notes.[226]

I began my study of Liebig's 1830 notebook by reviewing the interpretation presented by Usselman *et al.* The notebook contains about ninety numbered pages entirely devoted to organic analysis. Roughly the second half reports almost entirely alkaloid analyses, although some of the later pages contain analyses of other substances published in Liebig's 1831 paper. As Usselman *et al.* commented, none of the work is dated and there are no descriptions of experimental procedures. Their analysis suggested that the notebook covers about nine months, from spring to the end of December 1830, but that it provides only an incomplete record of Liebig's experimental work during this period. The notebook appears to have been

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[223] Liebig to Berzelius, 8 January 1831, in Lewicki 1991, 3.
[224] I have been most fortunate to have access to a microfilm copy of this notebook in the library at the Max Planck Institute for the History of Science in Berlin, as well as to the original held in the Bavarian State Library in Munich.
[225] Holmes 1987a, 132.
[226] L-W, letter 49, Liebig to Wöhler, 3 April 1831. Liebig may have had reason to refer here to the analyses of strychnine and brucine salts recorded in the 1830 notebook at folio 85v.

filled in generally chronological order although Usselman *et al.* inferred that some annotations were added at a later date, and occasional pages filled out of date sequence.[227]

The main use Usselman *et al.* made of the notebook was to propose an approximate date for Liebig's invention of the *Kaliapparat*, which they placed in early October 1830. They did this by noting the transition from volumetric to gravimetric determination of carbon, gravimetric analyses being made on samples of about 0.5-1.0 g, roughly five to ten times the mass of a typical sample for volumetric analysis. According to Usselman *et al.* gravimetric determinations of carbon necessarily resulted from "collecting effluent carbonic acid in an absorption tube filled with potash solution", i.e. in something similar to the *Kaliapparat*. They found that this transition was "absolutely sharp" and occurred at folio 43v, about half way through the notebook. They also placed Liebig's last volumetric determination of carbon a few pages later at folio 46v, which they interpreted as showing that Liebig was soon "more than satisfied by the reliability of the data from the new [gravimetric] method".[228] Despite this, Usselman *et al.* suggested that Liebig "may have needed some weeks to bring the full combustion apparatus to the sophisticated state described in his published paper". They reproduced a page from the notebook (folio 55av; Figure 7) showing a very rough sketch of a prototype *Kaliapparat* in which the five glass bulbs were arranged in a U-shape, rather than in their eventual triangular form.[229]

According to Usselman *et al.*, Liebig produced the *Kaliapparat* in something very like its final form within days of returning from his meeting with Berzelius in Hamburg in September 1830. He abandoned the existing volumetric method for carbon almost immediately because the results he obtained using his new apparatus were so good, yet he continued to make modifications to improve its performance over a period of several weeks. Could the notebook help decipher the details of this somewhat paradoxical tale of discovery? At first sight, I thought not. Liebig's sketch of the *Kaliapparat* soon emerged as one of the few readily comprehensible entries in the notebook. The pages reproduced here (folio 45v/46, Figure 8) are more typical: the *verso* page carries a relatively neat summary of the experimental results; the facing page is littered with unidentified calculations in random order. Many of the

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[227] Usselman *et al.* 2005, 7, fn. 20.
[228] Ibid., 9.
[229] Ibid., 7-12.

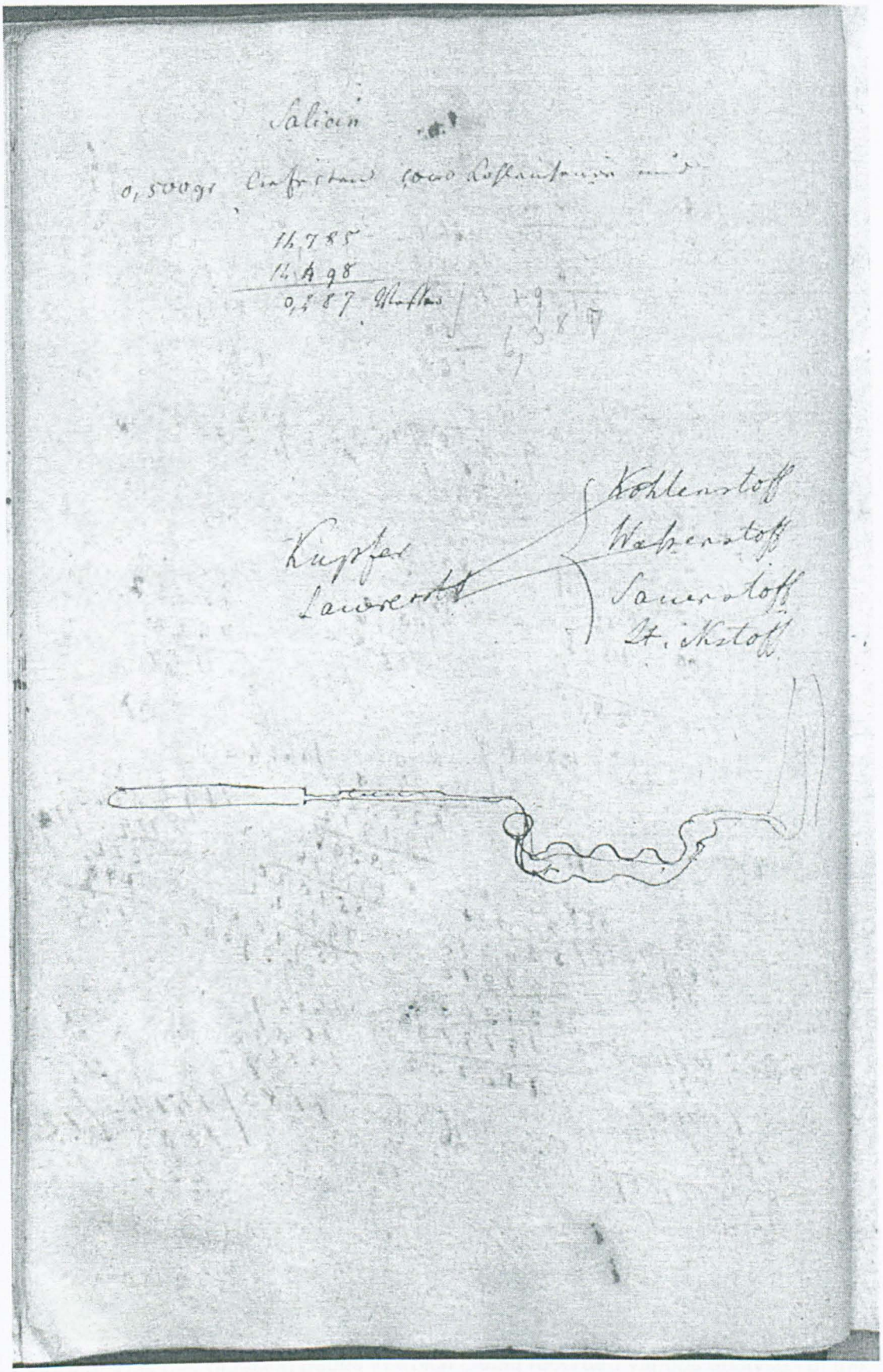



Figure 7. This unusual page from Liebig's 1830 notebook shows his sketch of a combustion apparatus including a prototype *Kaliapparat*. Liebigiana IC1, folio 55av, Bayerische Staatsbibliothek, Munich.

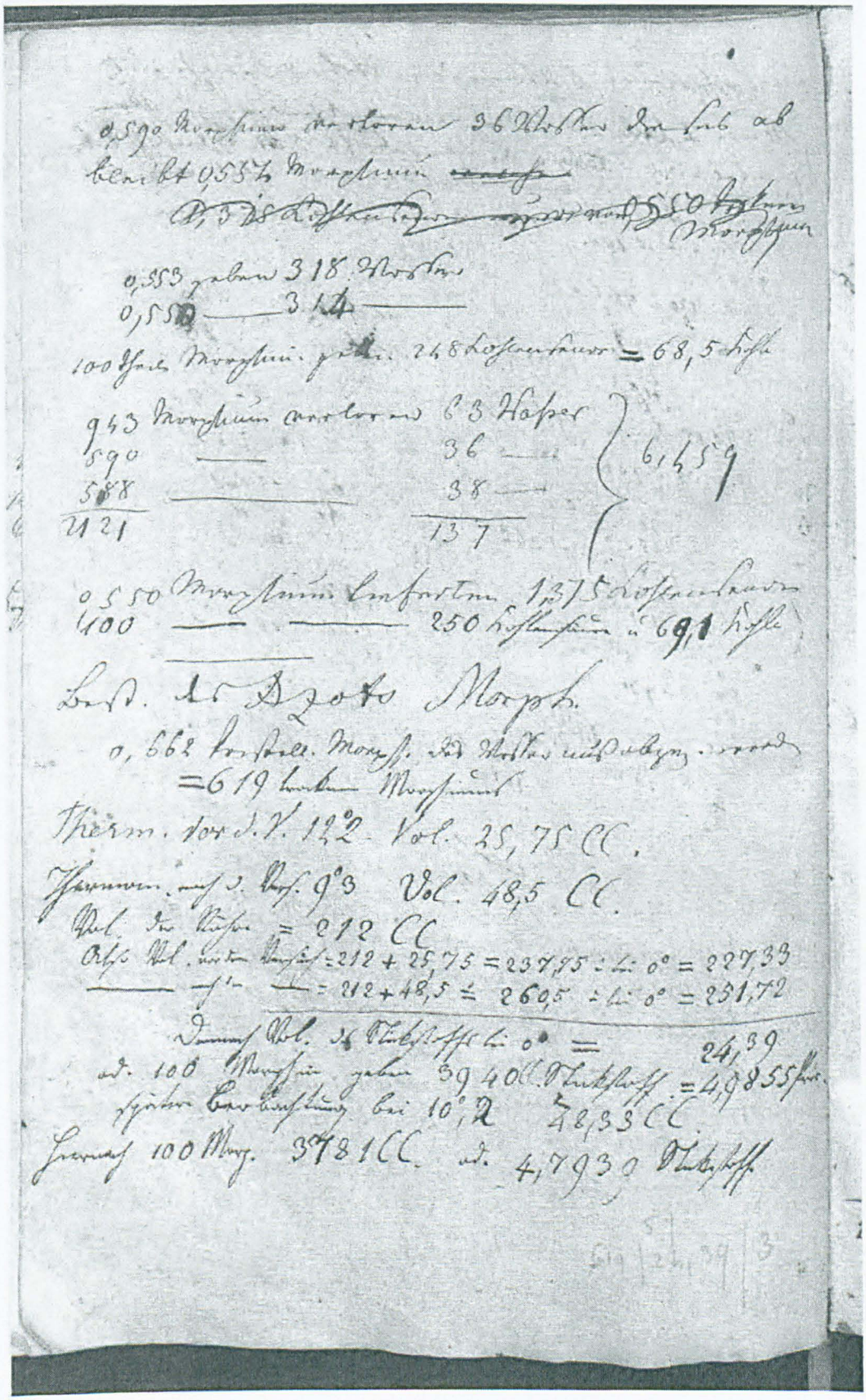
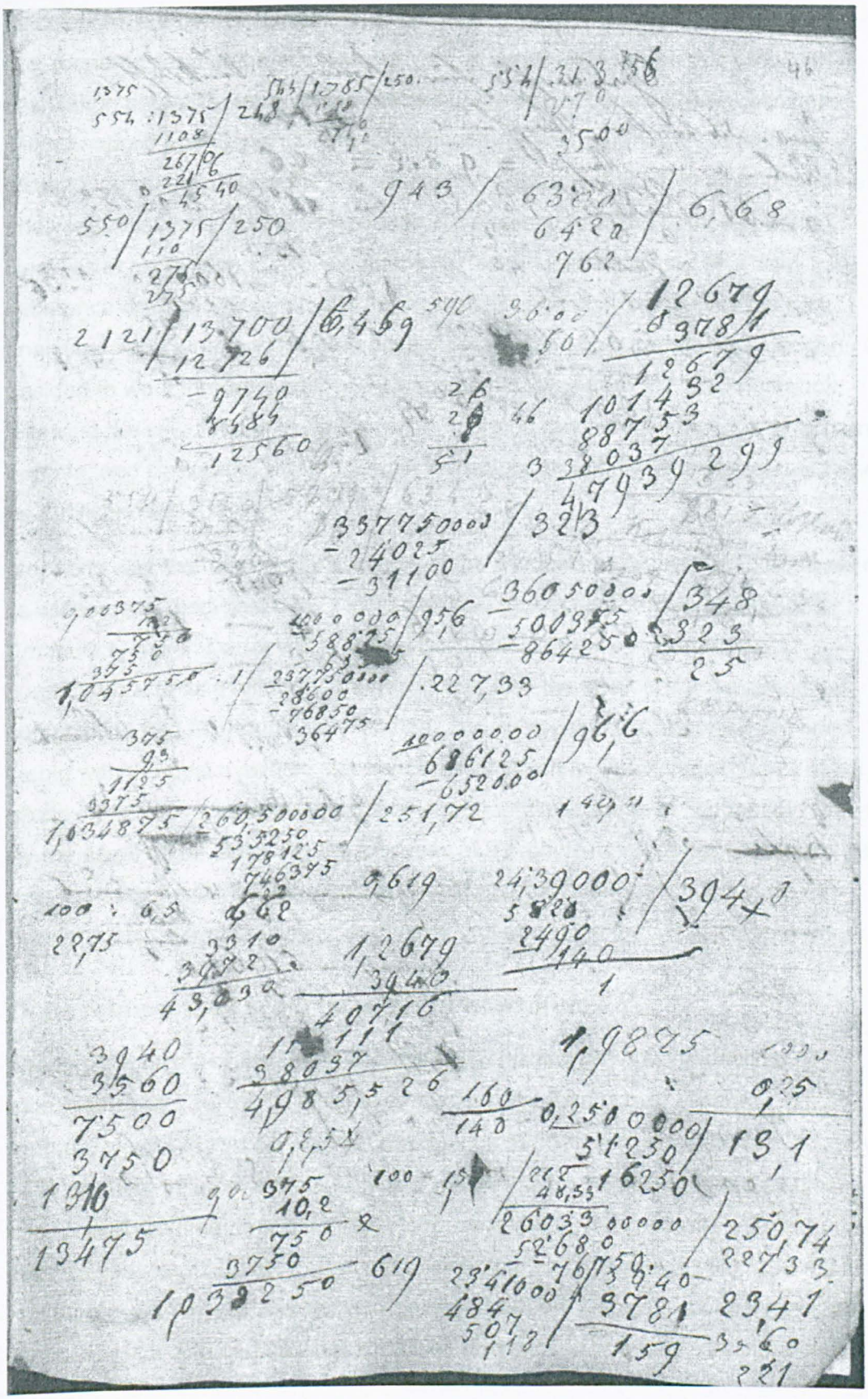


Figure 8. This pair of facing pages in which Liebig recorded various analyses of the alkaloid morphine are much more typical of what confronts the reader of his 1830 notebook. The *verso* page reports raw results of the determination of water, carbon dioxide and nitrogen, whilst the *recto* page (overleaf).



carries the calculations by which Liebig converted those results into composition. Liebig attempted to fit a formula for morphine to these results on the following page, where repeated alterations and crossings out indicate the difficulties he encountered. Liebigiana IC1, folio 45v and 46, Bayerische Staatsbibliothek, Munich

calculations are overwritten and they are made more difficult to follow by crossings out, roundings and arithmetical errors, as well as by Liebig's use of methods of calculation unfamiliar to anyone educated in the age of the electronic calculator. Then I noticed that Liebig's notebook concentrated on the analysis of just one alkaloid: morphine. It was the first alkaloid he analysed (folio 43v) and the one he analysed most frequently (see Appendix for a complete listing of these results). Here, as in his published alkaloid analyses, Liebig used morphine as a test substance against which to judge the capabilities and shortcomings of his new analytical apparatus, and his methods for determining both carbon and nitrogen. I decided to work through Liebig's analyses of morphine from his 1830 notebook, following the calculations by which he transformed raw results into composition and formula, and comparing what I found in the notebook with the analysis of morphine he published in 1831.[230]

Morphine was the most easily available of the alkaloids Liebig analysed because of its widespread medicinal use. Liebig obtained morphine from two pharmacists: Emanuel Merck in Darmstadt and Carl Wittstock in Berlin.[231] Partly as a consequence of its availability, morphine was also the alkaloid whose elemental composition had been most investigated. The composition of morphine provided Liebig with the best available standard against which to check the accuracy of his alkaloid analyses and to establish their superiority over those of Dumas and Pelletier. By the same token, following the analyses of morphine in the pages of Liebig's 1830 notebook seemed to offer the best available approach to reconstructing his development of the *Kaliapparat* and method of analysing the alkaloids as a whole.

## Determining the carbon content of morphine

The experimental results Liebig obtained from his first gravimetric analysis of morphine (folio 43v) fell far short of contemporary standards of accuracy. The reported weight of carbon dioxide corresponds to 55% by mass of carbon, roughly ¾ of the modern value of almost 72% and well below the values obtained by other chemists at the time. For example, the value given by Dumas and Pelletier in their 1823 paper was 72.02%.[232] The calculations on the facing page (44) included the first step in working out the percentage of carbon, but Liebig did not complete the process. He would certainly have realised that this intermediate value was much

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[230] Like Usselman *et al.* (2005), I have assumed that the notebook was filled in roughly chronological order.
[231] Liebig 1831b, 15.
[232] Dumas and Pelletier 1823, 191.

too low and abandoned the calculation, proceeding to repeat the determination of carbon on the following page (44v). The notebook shows that this repeat analysis was also based on the gravimetric determination of carbon content and that the results remained problematic. Whatever gravimetric method Liebig was using at this time, it failed to capture all the carbon dioxide produced in the combustion, with the result that the carbon content it produced was consistently too low.

Liebig persevered, recording two further gravimetric determinations of carbon (45v) from which he calculated the percentage by mass of carbon as 68.5% and 69.1%. These values were much closer to, but still below, the then accepted value, which helps make sense of Liebig's decision to perform a volumetric determination of carbon as a comparison. This analysis (46v) gave the percentage carbon as 72.0%, almost identical to the figure reported by Dumas and Pelletier in 1823. Usselman *et al.* noted that this was the last volumetric determination of carbon recorded in the notebook and they inferred from this that Liebig was now "more than satisfied by the reliability of the data from the new method", but I present evidence from the notebook which I argue is more consistent with an alternative interpretation.[233]

Although Liebig extended his analytical programme after this point to include other alkaloids including narcotine, nicotine, strychnine and cinchonine, he also returned to the analysis of morphine on at least three subsequent occasions before obtaining results he was prepared to publish. First, he carried out a gravimetric determination of the carbon content of morphine sulphate (53v), which gave the percentage carbon as 53.90% in the salt (equivalent to 69.1% in free morphine).[234] Then, recorded shortly after his sketch of the prototype *Kaliapparat* (55av), he made a volumetric determination of morphine's nitrogen content followed by a gravimetric determination of carbon (56v).[235] The calculations Liebig made using these results reflect his concern that the nitrogen determination was too low (discussed in more detail below) but they also suggest that Liebig remained unclear about the status of his previous gravimetric determination of carbon (45v).

According to this volumetric nitrogen determination (56v), the total volume of gas produced by 0.100 g morphine was 132.155 cc corrected to standard conditions (0° and 28" mercury, referred to hereafter as s.t.p.). Liebig carried out a large number of calculations (57), one of which produced a value for this volume using the results

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[233] Usselman *et al.* 2005, 9.
[234] I calculated the carbon content of the free base using Liebig's methods.
[235] This carbon determination (56v) was recorded in pencil below the nitrogen determination, the calculations for carbon overwriting those for nitrogen on the facing page (57).

of his earlier analysis of morphine (45v). According to that gravimetric determination of carbon, 0.100 g morphine produced 0.250 g carbon dioxide, equivalent to 126 cc. Liebig added to this the 3.78 cc nitrogen produced by 0.100 g morphine, obtaining a total volume of 129.78 cc, substantially lower than measured by his latest analysis. It is impossible to be certain but nevertheless reasonable to speculate that this finding, which confirmed that his previous (45v) gravimetric determination of carbon was too low, prompted Liebig to repeat the determination of carbon. This analysis of morphine – perhaps performed using a somewhat modified version of the *Kaliapparat* – was the first to give its carbon content as higher than 72%, and the first of only two gravimetric determinations of carbon Liebig reported for morphine in his 1831 paper. Liebig transcribed this result to folio 63v, where he reported morphine's carbon content as 72.38% and attempted to fit a formula to his results so far. Liebig was evidently not completely convinced by the outcome ($C_{34}H_{40/36}N_2O_6$), because he performed one final gravimetric determination of the carbon content of morphine (68v) together with a last analysis for nitrogen. These last two published gravimetric determinations of carbon (56v and 68v) enabled Liebig to confirm the carbon content of morphine as 72.3%, but only after very considerable numerical manipulation (69).[236]

This sequence of events suggests that the process by which Liebig arrived at the *Kaliapparat* was rather more involved and protracted than Usselman *et al.* claimed. The dramatic increase in the carbon determinations during his first few analyses of morphine indicates that Liebig was making substantial changes to his experimental method, and probably to the apparatus he was using. Indeed, we cannot rule out that Liebig began this series of gravimetric carbon analyses by using apparatus similar to that introduced some fifteen years earlier by Berzelius.[237] We know that

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[236] Liebig 1831b, 17. The published percentage carbon from these experiments averaged to 72.3 %. Liebig adjusted the mass of carbon dioxide (68v) from 0.960 g to 0.955 g before publishing, thereby decreasing the calculated percentage carbon from 72.7% to 72.3 %. These calculations were based on 27.63 % carbon in carbon dioxide, rather lower than the value 27.27 % which was frequently used by Liebig in the 1830 notebook. Liebig (1837b) gave the value 27.65 % (in the analytical tables appended after the main text). Liebig (1831b, 13) explained that he had used Berzelius' newest atomic weights and Poggendorff's recently calculated weights for carbon dioxide and nitrogen, which helps to explain some minor numerical discrepancies between the calculations in the notebook and the values Liebig published.

[237] In this method, carbon dioxide was collected in a bell jar over mercury containing a small, accurately weighed glass bulb. The bulb was filled with solid potassium hydroxide to absorb carbon dioxide gas, and it was removed and reweighed after 24 hours. The difference between the two gave the mass of carbon dioxide. The record of the weight of the potash tube in Liebig's notebook (43v) is as consistent with the use of this method as it is with the use of something like the *Kaliapparat*.

Liebig had discussed his planned alkaloid analyses with Berzelius in Hamburg, and it is reasonable to infer that he would have sought the advice of the older man regarding the problems he knew these analyses would present.[238]

These analytical results also suggest that Liebig's final volumetric determination of the carbon content of morphine (46v) played a rather different role than Usselman *et al.* proposed.[239] I claim that this volumetric determination – far from confirming the effectiveness of his new apparatus – demonstrated to Liebig that, though promising, it was still *not* trapping all the carbon dioxide produced on combustion and was therefore not producing results of publishable accuracy. Liebig's persistence in determining the carbon content of morphine until he obtained results somewhat higher than Dumas and Pelletier's previous value, moreover, indicates that he had reason to believe that *their* result was also too low. In other words, Liebig was satisfied by his data only when it accorded with his own, presumably at least partly theoretically inspired, expectations.

My claim that Liebig was not fully satisfied with gravimetric determinations of carbon until rather later than Usselman *et al.* suggested is corroborated by his published analysis of urea (Harnstoff).[240] This analysis, one of three Liebig presented to assure his readers of the reliability of the new method of analysis, had been performed specifically to discover whether nitrogen liberated during the combustion interfered with the absorption of carbon dioxide by the *Kaliapparat*, and hence with the accuracy of the carbon determination. Urea had the largest nitrogen content of all known organic substances and a relatively low carbon content, so any effect of nitrogen on the percentage carbon determined using the *Kaliapparat* would be particularly noticeable. This analysis was recorded in Liebig's 1830 notebook at folio 62v, between the two published carbon determinations for morphine, and it confirmed that the evolution of nitrogen gas during the combustion did not interfere with the operation of the *Kaliapparat* as it now existed. As soon as he had this confirmation, Liebig calculated morphine's carbon content from the gravimetric determination at folio 56v. The result (72.38%), confirmed by his second published carbon determination (68v), was more than 1¼% higher than any of Liebig's previous gravimetric analyses of morphine, well over the threshold of significance for fixing the number of atoms of carbon. It is, I think, a reasonable inference that

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[238] L-W, letter 30, Liebig to Wöhler, 12 October 1830.
[239] Usselman *et al.* 2005, 9.
[240] Liebig 1831b, 8. Analysis using the *Kaliapparat* gave the carbon content of urea as 20.7%, somewhat higher than a calculated value of 20.2%.

Liebig had been struggling to understand and remove the causes of the rather low values for carbon content produced by his earlier gravimetric analyses, and that he was only satisfied that this problem had been overcome at some point during this later series of analyses.

Given the lack of experimental detail in Liebig's 1830 notebook, it is unlikely that we shall ever identify the moment at which Liebig first used something resembling the *Kaliapparat* in its final form. The results he recorded, moreover, accord much better with the idea that Liebig gradually improved his new piece of apparatus during a period of well over a month than with any particularly well-defined moment of discovery. Usselman *et al.* suggested that Liebig may have developed the *Kaliapparat* from something resembling a U-tube, introducing additional bulbs to improve the absorption of carbon dioxide gas and as a means of testing whether the combustion apparatus was air-tight.[241] My exposure of Liebig's struggle to ensure complete absorption of carbon dioxide in the *Kaliapparat* is entirely consistent with their persuasive proposal, but the evidence I have derived from Liebig's notebook suggests that his new apparatus was probably not producing reliably accurate, publishable results until some time in November 1830. This extended period of development, moreover, agrees well with the timing of two letters written by Liebig in mid-November. In one, written to Wöhler on 18 November, Liebig referred to the extremely rapid rate at which he was performing analyses; in the other, written at around this time, he was sufficiently confident to describe his new apparatus to Poggendorff.[242] According to this account, inventing the *Kaliapparat* took weeks of painstaking work and, though it greatly simplified the experimental analysis of carbon content, it did not increase the accuracy of carbon determination above what was achievable by a skilled analyst using the existing method.

## Determining the nitrogen content of morphine

Liebig devoted a substantial part of the introduction to his 1831 paper to explaining why it was difficult to determine the nitrogen content of the alkaloids with the accuracy necessary to fix their composition, and to a description of the experimental methods by which he had attempted to overcome this practical analytical difficulty. This discussion is worth reviewing in some detail both in order to clarify the nature of the problems Liebig faced and because it contains a description of the three

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[241] Usselman 2005, 11-12.
[242] L-W, letter 34, Liebig to Wöhler, 18 November 1830, and the reply letter 35, Wöhler to Liebig, 28 November 1830, in which Wöhler referred to an earlier letter sent by Liebig to Poggendorff. Liebig's original letter to Poggendorff seems not to have survived.

experimental methods for nitrogen determination he used during his investigations. Because each of those methods produced results identifiably different in format, this information allowed me to infer which method of nitrogen determination Liebig had used from the results he recorded for morphine in the 1830 notebook. As I show below, the correlation of this information with the nitrogen determinations Liebig published in 1831 and with the nitrogen content he calculated for morphine provides a valuable and intriguing insight into how he accommodated his experimental results to his theoretical expectations. Liebig's analytical results were *not* independently decisive. Instead, he was able to assign the composition of morphine only by an intricate series of decisions about which results were likely to be the most accurate and what outcome was most theoretically acceptable.[243]

I mentioned above that Liebig published analyses of three substances of known composition performed using the *Kaliapparat* before continuing to the analysis of the alkaloids.[244] The first was an analysis of racemic acid (*Traubensäure*), which contains no nitrogen. This analysis was carried out by his student, Hess, and therefore not contained in Liebig's notebook. The second and third, performed by Liebig and recorded in his 1830 notebook, were of two nitrogen-containing substances: urea (*Harnstoff*) and cyanic acid (*Cyansäure*). Liebig used these two analyses to assess the limits of usefulness of the existing qualitative method of determining nitrogen. In this method, described in more detail above, the ratio of nitrogen to carbon was found by measuring the total volume of gas produced on combustion, then absorbing the carbon dioxide and measuring the remaining volume of nitrogen. Liebig used determinations of carbon made using the *Kaliapparat* to show that, whereas the qualitative method gave good results for urea and for cyanic acid, this was not the case for morphine and substances with similarly small nitrogen content.[245]

The essence of the problem was that even extremely small errors in the measurement of the total gas volume had a noticeable effect on the calculated ratio of nitrogen to carbon, making this much smaller even than it should be. In his published demonstration of this problem (modelled on calculations of a kind which first appeared in the notebook at folio 57) Liebig began by calculating the expected

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[243] Some of these decisions were theoretically informed and, to this extent, Liebig's analyses of morphine provide further confirmation of Klein's (2003) idea that theoretical conviction played an important role in the assignment of formulae.
[244] Liebig 1831b, 7-8.
[245] Ibid., 8-9.

total gas volume from the combustion of 0.100 g morphine.[246] This was composed of 3.608 cc nitrogen and 131.86 cc carbon dioxide. Liebig presented the volume of nitrogen as an average, but I have been unable to determine which results he averaged to obtain this value.[247] The volume of carbon dioxide was calculated using the gravimetric determination of carbon originally reported at folio 56v and re-calculated at folio 69. According to Liebig, 0.100 g morphine produced 0.260 g carbon dioxide, equivalent to 131.86 cc at s.t.p.[248] The total volume of gas produced on combustion was therefore 135.468 cc, the sum of 3.608 and 131.86. Next, Liebig compared this total volume with those obtained from three combustions of 0.100 g morphine, which he averaged to 132.071 cc,[249] i.e. 3.397 cc less than Liebig's earlier calculated value. Based on this total volume and the calculated volume of carbon dioxide, 131.86 cc, the calculated volume of nitrogen obtained would be 0.211 cc.[250] As a result of what appears to be an arithmetical error, Liebig calculated the volume of nitrogen to be about 0.7 cc, so that the apparent volume ratio of nitrogen to carbon dioxide was 1:190, well below the accepted value of 1:34.[251] As he explained in the 1831 paper, "if carbon [of the alkaloids] is determined as accurately as possible, then all the errors made in the quantitative determination of the gas volume, as well as errors of observation, fall on the calculation of nitrogen".[252] The development of the *Kaliapparat*, which gave a separate and reliable measure of carbon content, enabled Leibig to expose the unsuitability of the existing method for determining the nitrogen content of the alkaloids.[253]

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[246] Ibid., 9.
[247] I am unable to reproduce that calculation exactly. For example, if one averages the volumes of the three nitrogen determinations from Liebig (1831b, 17) the value obtained is 3.573 cc not 3.608 cc.
[248] I am unable to locate this conversion in the notebook. Liebig originally obtained 1.780 g carbon dioxide from the combustion of 0.680 g morphine (56v), but his later calculation (69) either adjusted or mistranscribed the mass of carbon dioxide as 1.770 g, from which he calculated that 0.260 g carbon dioxide were produced from 0.100 g morphine. The usual density of carbon dioxide used in Liebig's notebook is 1.97978 g/cc, according to which 0.260 g is equivalent to 131.32 cc.
[249] One of these values, 132.92 cc, was obtained in the analysis recorded at folio 68v. I have been unable to identify the sources of the other two results. I calculate the average of the figures Liebig reported as 132.048 cc.
[250] Liebig (1831b, 9) claimed that the reduction in the volume of nitrogen was 2.897 cc.
[251] Removing the numerical error makes this ratio 0.211:131.086 or 1:621.
[252] Liebig 1831b, 9.
[253] Liebig's notebook (57v) illustrated a similar problem in determining the nitrogen to carbon ratio in the opium alkaloid narcotine. Liebig obtained the ratio 1:75, considerably lower than Dumas and Pelletier's 1:20 and the modern value 1:22. Several of Liebig's 1831 nitrogen determinations for other alkaloids had been obtained in exactly this way. See, for example,

Liebig described two additional experimental methods for the determination of nitrogen in his 1831 paper. One, by means of which he claimed to have achieved more accurate results, was based on a direct measure of nitrogen content. In this method, Liebig passed potassium hydroxide solution through the combustion apparatus at the end of the analysis to absorb carbon dioxide. This process took a couple of hours, after which the volume of nitrogen was measured as the difference between the gas volumes before and after the combustion. This separated the determination of nitrogen from the determination of carbon (and hydrogen), thereby removing the link between the two measurements.[254] The main remaining problem in this analysis was to avoid the formation of nitrogen oxides, and Liebig explained that he had tried to avoid this by mixing the organic substance with partially reduced copper oxide.[255] The third method, which Liebig claimed to have abandoned and to have described merely in order to save others from similar fruitless attempts, used ammonia gas to remove carbon dioxide from the gaseous combustion products. This method, he explained, would rarely give reliable results because of the way the volume of the ammonia gas changed with changing temperature, and he presented one set of experimental results obtained for the cinchona alkaloid cinchonine to illustrate the problem.[256]

I located these results in Liebig's notebook (49v), and I found that they were quite distinct in format from results recorded for either of the other two methods. It was therefore something of a surprise to discover that two of the three nitrogen determinations Liebig published for morphine (44v, 45v) were based on results identical in format to these results for cinchonine. It was even more puzzling to notice that the percentage by mass of nitrogen given by Liebig for morphine in his 1831 paper had been calculated using only *one* of the three published results. This result (45v), moreover, seems to have been obtained by a flawed and, according to Liebig, discarded experimental method.[257] Explaining these findings is not easy, but Liebig's 1831 paper provides two possibilities: one practical, the other theoretical.

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the first of three nitrogen determinations for quinine on p. 25, found at folio 72v in the 1830 notebook.

[254] Liebig 1831b, 4. By 1830, the principle that accurate analysis required the separate determination of each element was widely accepted. See, for example, Henry and Plisson 1830, 97.

[255] Liebig 1831b, 9-11.

[256] Ibid., 11-12. We would now recognise this difficulty as resulting from the non-ideal behaviour of ammonia.

[257] Liebig (1831b, 16) reported that this sample of morphine, provided by Wittstock, had "smelt strongly of alcohol" when heated – a potential indicator of limited purity. Usselman *et al.* (2005, 8) described how Liebig obtained samples of purified alkaloids from a number of

Liebig emphasised that the greatest practical obstacle to the accurate determination of nitrogen in *any* substance remained the production of nitrogen oxides by the oxidation of nitrogen as a side effect of the combustion. One consequence of this was that the analyst could not simply average the values he obtained from repeated nitrogen determinations. He must instead "select from amongst those experiments during which a completely colourless gas is obtained, and those in which the mercury under the bell-jar in which the gas is trapped is completely un-corroded".[258] According to this, the results from combustion of any nitrogen containing substances which produced brown gas, or whose gaseous products attacked mercury, should be discarded as unreliable and, presumably, not published. The 1830 notebook shows that Liebig made seven attempts to determine the nitrogen content of morphine. It seems reasonable to infer that only three of these – the three he published in 1831 – produced completely colourless gaseous products.

One of these (69v), the final nitrogen determination in the notebook, had been carried out using Liebig's preferred, direct method. The measured volume of nitrogen (17.5 cc from 0.550 g morphine) was corrected to standard temperature and pressure (16.747 cc) by Liebig's usual method (70). From this, he calculated the volume produced by 100 mg morphine (3.134 cc) and converted this to the percentage by mass of nitrogen (3.9735%).[259] This value was substantially lower than Liebig had obtained from his earlier analyses and so, although he published these results, he did not use them in calculating the composition of morphine. Instead, this percentage nitrogen merely supported Liebig's inference that morphine contained 2 (and not 1 or 3) atoms of nitrogen.

Liebig's 1831 paper gave the composition of morphine as $C_{34}H_{36}N_2O_2$, and he drew attention to the fact that this was based on the largest of the three nitrogen determinations he had reported.[260] The important point for Liebig was that *all three*

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sources, returning those samples he found to be insufficiently pure. Liebig (1837b, 6) made much of the need to ensure that samples for analysis were absolutely pure, but he seems not to have followed his own advice on this occasion.

[258] Liebig 1831b, 10. The formation of nitrogen oxides during the combustion was visually apparent as brown fumes, whereas nitrogen is colourless.

[259] Liebig increased the corrected volume from 16.747 to 17.247 cc before calculating the volume of nitrogen as 3.134 cc. Liebig did not explain this amendment, though folio 70 contains a number of variations on this calculation suggesting that he wanted to see the effect of making small changes in the experimental values on the outcome. He also calculated the nitrogen to carbon ratio as 1:41, given that 0.100 g produce 0.260 g carbon dioxide equivalent to 131.3 cc.

[260] Liebig (1831b, 18) gave the composition of morphine as 2 atoms of nitrogen (4.92%), 34 atoms of carbon (72.20%), 36 atoms of hydrogen (6.24%) and 6 atoms of oxygen (16.66%), based on a combining weight of 3613.

nitrogen determinations had been significantly below the value (5.53%) found by Dumas and Pelletier.[261] Theory, moreover, required nitrogen to be present in a whole number of atoms, which meant that none of his nitrogen determinations supported fewer than two nitrogen atoms in morphine.[262] Given this, Liebig seems to have chosen to calculate the percentage nitrogen from the result closest to the theoretically expected value (about 5%) irrespective of which experimental method had produced this result. Viewed in this way, Liebig's decision to calculate the percentage nitrogen in morphine from his largest experimental value (4.995%) appears entirely rational.

One thing these nitrogen determinations make clear is that, despite the analytical advances it contained, Liebig's 1831 paper did *not* present a complete solution to the problem of alkaloid analysis. Liebig's introduction of the *Kaliapparat* undermined his trust in the existing method of nitrogen determination but he was unable to offer a fully satisfactory alternative. As Liebig admitted in writing to Berzelius, his recommended method of nitrogen determination was "tiresome, time-consuming and, in a word, quite unbearable", whilst the formation of nitrogen oxides during the combustion had driven him to "despair".[263]

How, then, should we interpret the results Liebig presented for morphine, and the way in which he used them to produce the alkaloid's composition and formula? Usselman, Rocke, and their co-authors have also noted that Liebig did not use all of his published analyses in calculating the elemental composition of several alkaloids, including morphine, but whereas the adjustment of the elemental composition to fit the combining weight was, they asserted, performed "under the guidance of theoretical allegiances", they considered that "his [Liebig's] examples of data selection are puzzling".[264] As Usselman observed in an earlier study, Liebig used only some of his published data in determining the carbon and hydrogen content of morphine, even though his selection "had no impact on the final result".[265] Liebig also selected from amongst his published data for nitrogen but – as I have just shown – this selection noticeably improved his results, making his analysis of morphine what Usselman called "the most accurate and impressive" of those he

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[261] Liebig 1831b, 18-19.
[262] Liebig's three nitrogen determinations were 4.51% (44v), 4.995% (45v) and 3.97% (69v). Only a value of around 2.5% nitrogen would have supported 1 atom of nitrogen in morphine.
[263] Liebig to Berzelius, 8 January 1831, in Lewicki 1991, 5.
[264] Usselman 2003, 82; and Usselman *et al.* 2005, 32-33.
[265] Usselman 2003, 85.

published.[266] Usselman *et al.* later suggested that Liebig's "implicit rationale was that the largest sample of morphine was likely to give the best values", but they came to no definite conclusion regarding Liebig's motives for any of these selections.[267]

I argue that these judgements remained problematic because they were being viewed in too narrow a context. Usselman *et al.* quite deliberately restricted the scope of their discussion to the determination of composition by elemental analysis.[268] Yet Liebig himself regarded the determination of composition and formula as wholly inextricable from the analyst's empirical experience and theories of constitution and reactivity. The raw results of experimentally valid analyses should be published, but especially for substances such as morphine it was impossible to produce a formula from these data *without* the exercise of subtle judgements.[269] I described above how practical experience and theoretical belief guided Liebig in his selection of just *one* out of his many nitrogen determinations as the basis for the composition morphine. Other aspects of Liebig's quest to produce a convincing and reliable composition – and hence formula – for morphine suggest that similar considerations were essential throughout his analytical practice.

Usselman *et al.* noted that Liebig prioritised combining weight over his analytical results when fixing composition, a choice which Liebig explained had required him to exclude the "several more pleasing proportions" for morphine consistent with his raw analytical data.[270] Although Liebig did not specify here his reasons for preferring other compositions, his first letter to Berzelius indicates that these were theoretically inspired. Berzelius was convinced that the alkaloids should behave like ammonia, and that nitrogen played a key role in their basicity. Liebig wrote that his experiments "fully confirm these views" even though, as he noted somewhat ruefully, the outcome might have been more striking had they proved exactly the opposite. As a result, Liebig continued, "my vanity must be satisfied that Nature does not adapt itself according to any individual idea".[271] In this instance, practical experience took precedence over Liebig's favoured theoretical outcome. But here,

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[266] Usselman 2003, 87.
[267] Usselman *et al.* 2005, 32.
[268] Ibid., 2.
[269] Liebig (1837b 37 or 1839b, 28) described his procedure for handling the "excess of hydrogen over the truth" of 0.14-0.2%. "In publishing the weights obtained in an analysis, we must ... give the numbers as they occur".
[270] Usselman *et al.* 2005, 33; Liebig 1831b, 18.
[271] Liebig to Berzelius, 8 January 1831, in Lewicki 1991, 4. Compare with Liebig's (1837b, 18) use of "individuellen Idee".

as elsewhere, theories of constitution and reactivity, particularly in relation to nitrogen, combined with Liebig's empirically based assessment of experimental reliability to provide the complex framework by means of which he produced meaningful chemical knowledge from empirically indeterminate analytical data.

The manner in which Liebig presented his analytical results for morphine may nevertheless strike us as somewhat disingenuous, particularly with regard to the method by which he arrived at its published nitrogen content, but we should not be too hasty to judge his behaviour as unscientific. Determining the composition and formula of morphine (and other alkaloids) was well beyond the limits of experimental accuracy in 1831 and remained so for many years to come. Making an accurate measurement of their nitrogen content in particular was known to be problematic and additional difficulties became apparent as many more analyses of all kinds of organic substances were performed in Liebig's Giessen laboratory during the 1830s. In 1838, Liebig considered the analysis of the alkaloids to be "one of the most difficult, one might say, an impossible task".[272] The "limit of accuracy" in the determination of hydrogen remained around 0.2% and, as Liebig explained in his somewhat irate response to Victor Regnault's recent alkaloid analyses, "whether [morphine] contains two atoms of hydrogen more or less, the analysis can give no information about this".[273] In such circumstances, "mere numerical results" would vary depending on who carried out the experiment, and Liebig insisted that the "true analysis" could only be distinguished from the "false" *by other means*.[274] Throughout the 1830s and beyond, the formulae of substances like the alkaloids were not produced from experimental data by simple deductive processes. Instead, the analyst called on his manipulative skill and experience, in combination with his chemical knowledge, to present the formula which gave the best possible fit with the available analytical results and prevailing theoretical expectations.

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[272] Liebig 1838a, 42.
[273] Wöhler and Liebig 1837, 13 ("die Grenze der Genauigkeit"); Liebig 1838a, 43. See also Regnault 1838.
[274] Liebig 1838a, 59. Even the requirement that any proposed formula must be consistent with the experimentally determined combining weight did not always distinguish effectively between various possible formulae – as Liebig (1838a, 42-43) claimed was the case for the formulae he and Regnault had assigned to morphine.

## The Determination of Nitrogen and the Standardisation of Organic Analysis

> *We strive without exception to achieve a common goal; a difficulty removed from the path is an advantage which does everyone good.*
>
> *Justus Liebig (1834)*[275]

If Liebig did not present his new method of analysis including the *Kaliapparat* as a complete solution to the problem of organic analysis, it was also not greeted as such, even by his closest supporters.[276] We know quite a lot about the reception of the *Kaliapparat*, and how its use to measure the carbon content of organic substances travelled through continental Europe, to Great Britain and even to the United States, but relatively little about Liebig's approach to the determination of nitrogen.[277] In this section I argue that although this aspect of Liebig's analytical method was central to his research during the mid-1830s, he struggled and ultimately failed to establish his approach to the determination of nitrogen as standard. The failure of other chemists, most notably Dumas, to adopt his experimental method for nitrogen or even, it appeared to Liebig, to understand *why* the determination of nitrogen remained problematic, involved him in continuing, public disagreements. These disputes draw our attention to the important but largely neglected role of the *Kaliapparat* in nitrogen determination according to Liebig's method. They also highlight Liebig's desire for *standardisation* of analytical practice.

Dumas, by now the leading exponent of organic analysis in France, first responded to Liebig's alkaloid analyses in a letter to Gay-Lussac printed in the *Annales de Chimie et de Physique* immediately after the French translation of Liebig's paper.[278] He began in apparently congratulatory vein, asserting that the new method of analysis "was destined without any doubt to change the state of organic chemistry within a very short time".[279] He continued, however, to undermine that compliment by expressing his opinion that "the analysis of an organic substance is easier and more certain than the analysis of a clay". The existing apparatus developed by Gay-Lussac and Liebig was largely responsible for that, he claimed, since all analyses could be executed with "sufficient precision", whilst most resulted in "perfect precision". The large variations in the results obtained by different chemists using different methods were, according to Dumas, mainly the result of analysing impure

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[275] Liebig 1834d, 172.
[276] See, for example, Berzelius 1832.
[277] Rossiter 1975; Rocke 2003; Usselman *et al.* 2005. See also Jackson (2006) on the importation of Liebig's method of analysis to Britain.
[278] Liebig 1831a.
[279] Dumas 1831b, 198.

samples and he still maintained that the purity of the sample had at least as much effect on the results as the method of analysis itself. Liebig's work, he said, had not changed his mind about that.[280]

Dumas' initial response also included a fierce critique of Liebig's recommended approach to the determination of nitrogen, which was based on a direct measurement of the volume of nitrogen produced by combustion. Liebig collected gaseous nitrogen and carbon dioxide together. Once the combustion was finished, he removed carbon dioxide by flushing the apparatus with potassium hydroxide solution, so that only nitrogen remained.[281] Shortly afterwards Dumas considerably moderated his criticisms, claiming that not having had diagrams of Liebig's apparatus had "given him a false idea of his [Liebig's] method", but he still asserted that his own apparatus and method was "simpler and more certain".[282] In particular, Liebig's apparatus necessitated at least six joints, in place of only two in his own – each additional joint increasing the probability that the apparatus was not airtight. His other main objection to Liebig's method for determining nitrogen concerned the moisture introduced with the potassium hydroxide solution Liebig used to absorb carbon dioxide. This would, he said, tend to increase the observed volume of nitrogen and, since the parameters affecting the extent of this error varied with each experiment, it was impossible to introduce a correction to take account of this problem. Dumas concluded by reinforcing the connection between the exactitude of analyses and the methods employed. At a time when instruments and methods of calculation were so perfect, he claimed, "one approaches the truth as closely as one wishes, when one uses absolute procedures and removes all causes of variable error". The implication was clear: in Dumas' opinion, Liebig's method for the determination of nitrogen did not meet these criteria.[283]

Somewhat surprisingly, given his privately expressed opinion about the reliability of Dumas' analytical chemistry and his encouraging response to Liebig's 1831 paper, even Berzelius did not regard Liebig's method for nitrogen as unquestionably the better of the two. According to his *Jahres-Bericht* for 1831, both methods were "approximately equally reliable".[284] Only Wöhler, who had by this time worked with Liebig on a large number of analyses as part of their investigation of the benzoyl

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[280] Ibid., 212.
[281] Liebig (1831b, 9-11).
[282] Rocke (2001, 44) suggested that Dumas' conciliatory attitude to Liebig at this time was motivated by his hope that Liebig would support his election to the Parisian Academy of Science.
[283] Dumas 1831a, fn. pp. 324-5.
[284] Berzelius 1832, 196.

radical, was prepared to support Liebig's method for nitrogen more strongly. In his opinion, included in an extensive footnote to his German translation of the *Jahres-Bericht*, the problems with Dumas' method became clear when one considered the purpose of the potassium hydroxide solution Liebig had used. Without this, Wöhler reasoned, some carbon dioxide must remain in Dumas' apparatus, some of which would be measured as nitrogen. For substances such as the alkaloids, which contained very little nitrogen, Wöhler suggested, this error might double their nitrogen content. Wöhler concluded rather bluntly by noting that, although such an error would not have escaped Dumas' perspicacity had he *tried* to make a nitrogen determination using this apparatus, no analysis of this kind had been made public by Dumas since his analysis of fulminating gold (*Knallgold*). In other words, Wöhler did not believe that Dumas had ever attempted such an analysis.[285]

Liebig shared this view, and he gave vent to his frustration in a letter to Berzelius, which he sent unsealed *via* Wöhler in December 1831:

> *What have you said about Dumas' notes on my work about the plant bases? It is certainly ludicrous to publish an apparatus, which he imagines himself to have discovered, for the one which he calls his own has never been constructed or applied by him. The apparatus which he publishes as his own is not usable and gives completely incorrect results, because more carbon dioxide remains in the combustion tube than several organic bases contain. But if I forgo the foolishness of saying something against it and of uncovering the error in his apparatus, then he is in a position to make known a drawing of an apparatus and to publish it as his own, in which all criticized errors are avoided, and I stand there like a cat drenched in water. His fate will soon catch up with him.*[286]

Disagreement between Liebig and Dumas about the best method of determining the nitrogen content of organic substances flared again in 1834, a year after Dumas had published a new, direct method for determining nitrogen.[287] The principles of Dumas' new method were very similar to those recommended in 1831 by Liebig: carbon dioxide produced in the combustion was absorbed by concentrated potassium hydroxide solution, so that only nitrogen gas was collected over mercury. "The only precaution to be observed", Dumas claimed, was that at least 30-40 cc nitrogen gas should be obtained.[288] In Liebig's opinion, however, Dumas' new method "has the same defect as all earlier [methods]" because Dumas had not taken any steps to avoid the formation of nitrogen oxides during the combustion,

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[285] Ibid. See also Wöhler's fn. to that page.
[286] Liebig to Berzelius, 28 December 1831, in Lewicki 1991, 25.
[287] Dumas 1833.
[288] Dumas 1834, 75.

identified in 1831 by Liebig as the most important barrier remaining to the accurate determination of nitrogen.[289]

Liebig also noted that, although Dumas had determined the carbon content of picric acid (*Kohlenstickstoffsäure*) using the *Kaliapparat*, he had not used this gravimetric determination of carbon to test the validity of the qualitative analysis for nitrogen he also reported. Both methods should give the same percentage carbon and where they did not, this implied an error in the qualitative analysis. Had Dumas tested his results in this way, Liebig argued, he would have found a large discrepancy between the two carbon determinations. Dumas had adopted the use of the *Kaliapparat*, but he had either not understood or chosen to ignore one of its most important purposes. "An error in the qualitative analysis", Liebig explained, "repeats itself in the quantitative. [...] The removal of this great uncertainty in the analysis of nitrogen containing substances was for me the main object of my recent investigation of the organic bases."[290]

Liebig was clearly frustrated that Dumas persisted in neglecting the hard-won insights produced by his investigation of the alkaloids. Moreover, the fact that outcomes Liebig regarded as important were not being taken seriously by his rival was not just a personal slight. Liebig believed that because Parisian chemists had not accepted and applied his methods for determining the composition of nitrogen-containing substances they continued to publish unreliable analyses, which made no useful contribution to the discipline. Pelletier and Couerbe, for example, had recently determined the very low nitrogen content of the organic bases menispermine and paramenispermine by Gay-Lussac's method, which Liebig explained had already been proved to give "completely inexact results" for substances containing little nitrogen.[291]

For Liebig, establishing a standard method for determining the nitrogen content of organic substances was a necessary intermediate step towards his much more ambitious goal of understanding natural processes through organic chemistry. Whilst his students worked to incorporate the *Kaliapparat* into a pedagogically stable method of quantitative analysis for non-nitrogenous substances Liebig pursued the analysis of nitrogenous compounds, and in 1834 he published a series of papers in which he set out a manifesto for his analytical approach to the study of chemical and biological transformations. I contend that these papers were an attempt to get other

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[289] Liebig, fn. pp. 82-84 to Dumas 1834, 84.
[290] Liebig, fn. pp. 82-84 to Dumas 1834, 83-84.
[291] Liebig 1834b, 209.

chemists, and particularly those in Paris, to hear his message and adopt his methods. Opening the first paper, Liebig explained that:

> *The investigation and description of pre-existing organic compounds, no matter how important this is in and of itself, leads to little certainty about the laws according to which changes and decompositions in organic nature occur; we must try to research these transformations above all and in this connection in organic chemistry only the analytical way can lead to the goal.*[292]

This was because "only elemental analysis can give security to the operation, can give certainty to the consequences and conclusions",[293] and Liebig was convinced that chemists' "insight into the most secret processes of the nutrition etc. of animals [...] will gain a quite different meaning, [...] when we [...] follow its changes and transformations step-by-step through elementary analysis".[294]

Liebig presented the analysis of a number of nitrogen-rich substances including melamine in this paper. He continued to use finely divided copper in an extremely slow combustion to avoid the formation of nitrogen oxides, but Liebig now also adopted Dumas and Pelletier's method for removing air from the combustion apparatus. According to Liebig: "The adequately sharp controls which I have been able to apply to these bodies left me in no doubt that all other less simple ways were superfluous."[295] Just as in his 1831 analyses of urea and cyanic acid, Liebig's approach involved comparing the results of a qualitative analysis for nitrogen with the results of direct carbon determination using the *Kaliapparat*.[296]

The same approach was advertised in the following paper reporting Liebig's latest analysis of uric acid (*Harnsäure*). Lamenting that the many available analyses did not agree with one another, Liebig explained the cause of this discordance. Because chemists had not carried out a direct determination of carbon, such as that produced by the *Kaliapparat*, "they lacked a control for the determination of nitrogen, which the apparatus ... I have described, now reliably provides".[297] In the analysis of nitrogenous substances, Liebig claimed, only the correct application of the *Kaliapparat* as a means of *testing* the outcome of a qualitative analysis would enable analysts throughout Europe to produce reliable and comparable results.

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[292] Liebig 1834g, 1.
[293] Ibid., 2.
[294] Ibid., 3.
[295] Ibid., 13.
[296] See Liebig (1834g, 20) for a description of this method applied to melamine.
[297] Liebig 1834a, 47.

Liebig completed this series of papers with a revised analysis of hippuric acid, which he had first attempted to analyse in 1829, and he did so just in advance of Dumas.[298] Liebig explained the faults in his earlier analysis:

> *I did not determine the carbon directly in the analysis of hippuric acid, since the apparatus which now serves that purpose only came into use later; it has further been proved by experience, that during the combustion of nitrogenous materials, if nitrogen and carbon are determined by volume [i.e. by a qualitative analysis], this method gives a small excess of carbon; apart from this, my first analysis gave less hydrogen than the theoretical composition assumed.*[299]

His new analysis, performed using his "now perfected apparatus", gave the formula of hippuric acid as $C_{18}H_{18}N_2O_6$.[300] Liebig may have been pleased that the *Kaliapparat* was in widespread use, but this series of papers gives the impression that he would only be truly satisfied when every analyst also used a gravimetric determination of carbon to check the accuracy of their qualitative analyses for nitrogen.

## Liebig's *Introduction* and the Dissemination of a standard, pedagogically stable Method of Organic Analysis[301]

> *Professor Liebig is universally acknowledged as the leader in the rapid march of organic chemistry. It is chiefly to the use of his method, as described in this work, that the sudden development of this department of science must be ascribed; but he is not only the great improver of the method, he is also the author of very numerous memoirs, in all of which he has displayed uncommon sagacity, united with the most rigid accuracy; and any one of which might serve as a model of chemical research. While, therefore, it would be unjust to deny an almost equal share of merit to those philosophers, both in France and Germany, who have so ably cultivated the same field, we cannot hesitate in regarding Professor Liebig as the first authority on the subject of organic analysis.*
>
> *William Gregory (1839)*[302]

Liebig's *Introduction to the Analysis of Organic Bodies* (referred to hereafter as the *Introduction*) has often been presented as the textbook manifestation of his 1831 method of analysis, which makes the fact that it was not published until 1837 rather a puzzle. The *Introduction* certainly contained a far greater level of practical detail than Liebig's 1831 paper and this has made it a useful source of information about

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[298] According to Geiger, Liebig's work had been completed on 5 August, almost two weeks before Dumas and Peligot's (1834) analysis of hippuric acid.
[299] Liebig 1834e, 20.
[300] Liebig (1834f, 573) referred to his "jetzigen vervollkommneten Apparaten" in this note from Giessen, dated 18 August 1834.
[301] Liebig 1837b translated by William Gregory as Liebig 1839b. Quotations are taken from Gregory's English translation, except where otherwise indicated.
[302] Gregory 1839, iii.

how Liebig performed those earlier analyses.[303] For example, it included detailed instructions for how to produce a *Kaliapparat* by glassblowing. Nevertheless, as I argue in this section, the experimental practice described in the *Introduction* differed in important respects from Liebig's original 1830 investigations. Liebig's private research technique was transformed in the *Introduction* into a standard, pedagogically stable method of organic analysis but I show here that this did not merely entail the provision of greater experimental detail. Difficulties in the practice of organic analysis extended well beyond the choice and execution of a particular experimental method, encompassing the ability to distinguish "trust-worthy" from "erroneous" analyses and the complex sequence of calculations, corrections and adjustments by means of which the analyst was able to "discover" the formula of the substance under investigation.[304] Giessen analysts learnt to incorporate all these skills into their standard analytical practice and I contend here that the dissemination of these skills was one of Liebig's main objectives in publishing the *Introduction*.[305]

Liebig claimed in his *Preface* that the book was published at the request of many of his friends, specifically for use by them and their pupils in the laboratory, and the book's contents broadly support this purpose.[306] The *Introduction* provided extensive descriptions of the apparatus and techniques of organic analysis, including the determination of molecular weight using Dumas' method of vapour density measurement, which Liebig had adopted as late as 1834 and which was central to the production of formulae from analytical data.[307] Organic analysis involved quite extensive numerical work and Liebig included a series of numerical tables to assist in the calculations needed to convert raw analytical data into composition.[308] He also gave clear guidance on which substances were suitable for beginners and which not. The combustion of volatile liquids, for example, was characterised as being the easiest and giving the most accurate results, so that "beginners will do well to occupy themselves first with the combustion of such substances".[309] Analysing nitrogen-containing substances, on the other hand, was

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[303] For example, by Usselman *et al.* 2005.
[304] Liebig 1839b: 24 (trust-worthy), 37 (erroneous), 28 (discover).
[305] Liebig was especially keen throughout the *Introduction* to discredit Mitscherlich's modification of his method of analysis (discussed more fully in Chapter Four).
[306] Liebig 1837b.
[307] Liebig to Berzelius, 22 July 1834, in Lewicki (1991, 93) described Liebig's realisation that Dumas' results, although "not analytical" – i.e. not based on analytical investigation – were better than his own.
[308] Liebig included two copies of these tables, one unbound so that it could be taken into the laboratory.
[309] Liebig 1837b, 22-3 and 1839b, 18.

definitely *not* suitable for inexperienced analysts.[310] Even in 1837, the direct determination of a small nitrogen content required a "special operation" and remained subject to "a constant error, which is unavoidable".[311]

The pedagogical orientation and clarity of the *Introduction*, as well as its completeness and restricted scope, differentiated Liebig's textbook from other, earlier accounts of the same techniques.[312] Liebig included hints about the visible criteria according to which a combustion could be judged as successful or failed. If, for example, the sample "when one part of it has been ignited, continues to burn spontaneously, [...] the analysis is good for nothing".[313] Of particular importance were the extremely detailed instructions regarding error limitation, the controls to be applied to analytical results and how those results should be used in the production of formulae. In the case of carbon and hydrogen, Liebig claimed that all sources of error could be managed by following the recommended procedures. Substances of low atomic weight were straightforward, because it was easy to establish the number of atoms of each element. For substances with higher atomic weights, however, "a trifling difference in the determination of the atomic weight sometimes corresponds to more than half an equivalent of carbon, and often to more than 3 atoms, or 1½ equivalents of hydrogen". Here the analyst should check his results by comparing the outcome of analyses carried out in different ways to see whether or not the results were consistent.[314]

Liebig concluded by providing several example analyses in which analytical data, together with atomic (combining) weight, were used to arrive at a formula for the substance.[315] In his first example amygdalic acid Liebig assigned the formula $C_{40}H_{52}O_{24}$ but – as expected for a substance with high atomic weight – this was by no means the result of simple deduction from experimental data. A straightforward calculation based on the raw experimental results suggested that amygdalic acid contained 54 hydrogen atoms, which corresponded to a theoretical percentage

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[310] Liebig (1837b, 40 and 1839b, 32) noted that the combustion of a nitrogen-containing substance took twice as long as normal, whilst (1837b, 41 and 1839b, 33) explained that the various methods for determining nitrogen were "more or less simple according to the amount of nitrogen present". The description of these various methods required 14 pages of this 72-page book.

[311] Liebig (1837b, 48-49 and 1839b 37-38) described an adapted version of Dumas' 1833 method.

[312] C.f., for example, Dumas 1835.

[313] Liebig 1837b 28 and 1839b 23.

[314] Liebig 1837b, 53-55 and 1839b, 42-3.

[315] The term *Atomgewicht*, translated by Gregory as *atomic weight*, was used by Liebig in 1837 to refer to what in 1831 he had called the *Mischungsgewicht* or *combining weight*, i.e. the molecular mass of modern chemistry.

hydrogen of 4.99%, almost identical to the experimental value of 5.014%. As Liebig explained, however, "this *exact* coincidence proves the substance to contain *less* hydrogen than that formula indicates", and he therefore adjusted the number of hydrogen atoms to 52.[316]

This exemplified a persistent problem in the analysis of organic substances, and one worth clarifying because it became the subject of bitter controversy in the late 1830s examined in the following section. Liebig's *Introduction* summarised the problem:

> *By following, therefore, the process of analysis recommended in this work, we must always be prepared for an excess of hydrogen over the truth, amounting to from 0.14 per cent. to 0.2 per cent; and we can only consider the determination of the hydrogen as exact, when this excess does not exceed 0.2 per cent. When the analysis, without the above correction, gives exactly the theoretical quantity of hydrogen, there is much reason to doubt the accuracy of the experiment; and the formula found for the composition of the substance is erroneous, when the results of repeated analyses yield constantly less hydrogen than the formula indicates.*
>
> *In publishing the weights obtained in an analysis, we must not make the above deduction, but give the numbers as they occur, since the amount of excess, due to hygrometric water, furnishes to the reader a valuable means of judging of the accuracy of the determination of the hydrogen. It is only in calculating the composition with a view to discover the formula that we are to make the correction above mentioned.*[317]

In other words, a reliable analysis gave a percentage hydrogen 0.14-0.2% higher than demanded by the assigned formula, this excess being due to the presence of water in the sample. In no circumstances was it permissible for the analyst to assign a formula containing *more* hydrogen than found by experiment.

It is also interesting to note that, despite the lengthy section he devoted to the determination of nitrogen, none of Liebig's exemplar substances contained nitrogen. He used caffeine, an alkaloid with the unusually high nitrogen content of almost 29%, to demonstrate two alternative methods of calculating the results of a qualitative analysis for nitrogen, but included no experimental results at all in his description of the trickier direct method to be followed for substances whose nitrogen to carbon ratio was found to be 1:8 or less.[318] This threshold ratio was substantially smaller than the 1:5 Liebig published in 1831, suggesting that the techniques of qualitative analysis for nitrogen had improved during the previous six years. The *Introduction* shows, however, that the fundamental problem of nitrogen determination remained unsolved: without extreme attention to experimental precautions, nitrogen was converted into nitrogen oxides. "*The more carefully and intimately the mixture with*

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[316] Liebig 1837b, 58-61 and 1839b, 45-48. Emphasis in original.
[317] Liebig 1837b, 37 and 1839b, 28.
[318] Liebig (1837b, 45 and 1839b, 35) reported the analysis of caffeine.

*the oxide of copper has been made, and the more slowly the combustion is made to proceed*", Liebig emphasised, "*the less danger is there of the formation of the deutoxide of nitrogen*", but there was no sure way to prevent this completely.[319] Where there was evidence of the formation of nitrogen oxides, moreover, it was "not worth while [...] to finish the experiment: it teaches nothing, gives rise to false notions of the composition of the substance; and only raises doubts of the accuracy of the next better analysis".[320] Even in 1837, the analysis of any nitrogen-containing substance required a high level of manipulative skill, and the experience to know which analytical results were worth retaining. Small nitrogen contents measured by direct determination, moreover, had to be calculated as the average of two experimental values, one of which was *known* to be too high, whilst the other was too low.[321] Liebig went to considerable lengths to set out all the necessary procedures and corrections as clearly as possible, but the determination of nitrogen was still a demanding and highly uncertain process.

The method of analysis presented in the *Introduction* was not identical to that described by Liebig in 1831. In the case of nitrogen determination, the textbook proposed substantially different experimental methods, but even the determination of carbon and hydrogen included novel experimental controls and corrections. The *Introduction* therefore provides a useful insight into the nature of the work done by Liebig and members of his research group to transform the personal investigative technique Liebig applied in his alkaloid analyses into a reliable, pedagogically stable method for large-scale research. The analytical practice Liebig described in 1837 included significant new elements, many of which were the product of large-scale collective investigation in his Giessen laboratory. In the determination of hydrogen, for example, Liebig based his claims on "[i]nnumerable experiments" and "[d]aily experience".[322] Liebig was only able to write this textbook *after* research into and teaching of organic analysis were established in Giessen and one consequence of this is that, far from being unreasonably delayed, it could hardly have been published *before* 1837.

Historians have tended to emphasise the *Introduction*'s role in spreading the use of the *Kaliapparat* to other locations. This was certainly important, particularly in the case of countries like Great Britain where the practice of analysis was rather

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[319] Liebig 1837b, 41 and 1839b, 32. Emphasis in original.
[320] Liebig 1837b, 43 and 1839b, 31.
[321] Liebig 1837b, 50 and 1839b, 38.
[322] Liebig 1839b: 27 ("innumberable experiments") and 31 ("daily experience").

backward, but I suggest that by the time of its publication in 1837 the *Introduction* was at least as important for the guidance it contained regarding the management of errors and the processes by which the analyst could produce reliable formulae.[323] We know from earlier studies that the practice of carbon determination using the *Kaliapparat* travelled through Europe quite rapidly by personal contact, so that by 1837 it was already in use in all the major centres of chemical research.[324] What was not yet widely shared, as the disputes between Liebig and other chemists described below demonstrate, were the indicators of a trustworthy analysis, and the acceptable and productive methods of handling indeterminate experimental results. Disseminating *this* kind of information was, I assert, one of Liebig's principal objectives for the *Introduction*, reflected in both its timing and its content.

## The Giessen Approach to Organic Analysis

> *I hold it to be not difficult to discover a new crystalline substance, and still easier at the present time to perform an exact analysis on it; but I regard it as a real problem to cause such a substance to speak, to make it tell from what it descends, and who are its relatives.*
>
> *Justus Liebig (1839)*[325]

In this section I use two disputes from the late 1830s to reinforce and draw together the main themes of this chapter. How did Liebig and others in his Giessen laboratory incorporate the use of the *Kaliapparat* into a teachable method of organic analysis, and how did this relate to Liebig's vision of chemical research? How did analysts in Giessen learn to select results for publication, and as the data from which formulae could best be produced? Analysis might be "the only safe reagent" of organic chemistry, but analysis alone was rarely sufficient to determine composition and gave at best circumstantial support for chemists' constitutional theories.[326] Certainty was hard-won and often illusory. Whereas new inorganic substances could be assigned their place within a well-ordered taxonomy, it was much harder to classify organic compounds whose composition, constitution and chemical behaviour were so much less well understood. Nevertheless, Liebig considered organic substances were "links in one and the same chain, of which to date we could follow only a small stretch here and there".[327] It ought to be possible to place organic substances within the same taxonomy as inorganic, but neither

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[323] Gregory (1839, iii) confirmed that "for a good many years previous to 1836, no organic analyses were published by any British experimenter".
[324] Rocke 2003.
[325] Liebig 1839a, 314.
[326] Liebig 1834d, 173.
[327] Liebig 1834g, 2.

analysis on its own, nor the study of chemical properties in isolation could achieve that goal. In the context of chemical transformations, analysis could be used to provide "complete certainty" about the composition of a substance, as Liebig and Wöhler had done for benzoic acid.[328] Liebig believed that the practice of analysis in isolation produced results which could be badly misinterpreted and, as I describe below, he fiercely disputed the results of many such analyses during the 1830s.[329]

What exactly did Liebig consider differentiated research from the mere analysis? His Scottish pupil and champion William Gregory considered that any of Liebig's "very numerous memoirs [...] might serve as a model of chemical research", but this crucial topic was also one Liebig addressed directly in many of his publications. His protracted and heated disagreements with the Danish chemist William Zeise and Hermann Hess in St Petersburg in particular prompted Liebig to spell out in great detail how the analyst should follow "the only and true way, the way of elementary analysis".[330] These disputes have tended merely to provide historians with additional evidence for Liebig's hot headed and argumentative personality but I argue instead that they stem from his rapidly increasing sense of frustration at the analytical practices of his peers.[331] By the time these disagreements reached their peak in the late 1830s, Liebig had been vigorously promoting his approach to organic analysis through the pages of the *Annalen* for half a decade, but it was proving difficult to convince the European chemical community – or even his German colleagues – to follow his lead. Chemists were flocking to his Giessen school from far and wide but the example of Hess, who was a distinguished chemist and member of the Academy of Science in St Petersburg, shows that propagating the common research approach Liebig considered so important was no simple matter. Even in St Petersburg, to which one of Liebig's best students Aleksandr Woskresensky had recently returned, the message was just not getting through.

Liebig's dispute with Hess grew out of a well-known episode, which I briefly review here. In 1837 Liebig and Berzelius became engaged in a public disagreement concerning the relative merits of cork and the rubber-like substance caoutchouc for the connection of the various pieces of glassware forming the combustion apparatus.

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[328] Wöhler and Liebig 1832, 472.
[329] See, for example, Liebig's (1833, 618) critique of Döbereiner's analysis of acetal.
[330] Liebig 1834d, 173.
[331] Klein's (2003, 180-184) treatment of the early stages of Liebig's dispute with William Zeise is an important exception to this trend.

Berzelius favoured caoutchouc, which Liebig rejected.[332] As he explained in the *Introduction*, only cork neither absorbed nor gave up moisture during the analysis and so had no effect on the determination of hydrogen. In 1838 Hess entered the debate on Berzelius' side when he published the results of direct experiments suggesting that the weight of cork increased during combustion analysis because it absorbed water. His claims elicited an immediate response from Liebig.[333] Liebig defended the use of cork, but he soon broadened the scope of the argument to include the proper approach to research in general. As a result, these remarks appeared so important to Gregory that he transcribed them in full in a lengthy footnote inserted in his 1839 English translation of the *Introduction*. According to Gregory:

> *They place the question [of whether to use cork or caoutchouc] on its proper footing; and the admirable researches which daily proceed from Professor Liebig's laboratory, not only those of Professor Liebig himself, but those of numerous pupils, as M. M. Ettling, Schoedler, Fehling, Thaulow, Woskresensky, Gros, Regnault, Demarçay, Richardson, Campbell, &c., clearly prove the sagacity of the founder of such a school, and the great advantages derived from a simplification of the apparatus, which enables any one with ordinary care to perform an accurate analysis.*[334]

Gregory's comment neatly captures the three main strategies Liebig used to dispute Hess's findings. First, Liebig himself "had made the experiment described by my distinguished friend [Hess] a great many times", in other words his *personal experience* far exceeded Hess'. Second, he drew on the *collective experience* of his research school, claiming that:

> *The opinion which I have expressed in the work on Organic Analysis [the* Introduction*], is founded on experience, derived from all the organic analyses which have been made by all the different experimenters in this department, the number of which must amount to several thousands.*

Finally, Liebig made a powerful plea for using the simplest possible apparatus, which alone made possible the *vast numbers of analyses* necessary for the kind of research by means of which organic chemistry could make progress.

> *Progress in organic chemistry is out of the question, without researches; but these include not the analysis of a single substance, but of a series of products; 60-70-100 or more analyses are not rare in the course of one investigation of this kind. I obtain in one experiment a substance of peculiar properties, which I analyse. I again procure it under somewhat different circumstances, and observe differences in the second analysis. In a third I observe further discordance; at last I arrive at the knowledge of a substance, whose properties are uniform, and whose composition explains the*

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[332] Liebig 1837b, 38-39 and 1839a, 29. Unusually and probably for reasons of diplomacy Gregory's translation diverges from Liebig's somewhat intemperate original.
[333] Hess 1838. Liebig responded in an extended footnote, pp. 192-4.
[334] Liebig 1839b, 29. Gregory's footnote extended over pages 28-30.

> *discordance of the first results. The last analysis alone is published; the others were merely* tests.

Liebig's claim to authority ultimately rested on the huge volume of work performed in his Giessen laboratory, by him and the members of his research school, using simple apparatus. Far from claiming superior accuracy for his method of analysis, Liebig celebrated the fact that: "Our analyses are no worse than those of the chemists who employ an apparatus constructed to insure mathematically accurate results, *which however it does not give.*" Rather, "the advantage of our methods does not consist in greater accuracy, for, as we have seen, the old method was susceptible of the greatest exactness, but in the greater simplicity and security, with the same degree of exactness, which they afford". "[I]n Paris and in [St] Petersburgh", Liebig continued, "it is not thought worth while to invent new and perfect apparatus; doubtless because chemists there go practically to work; for which, among us, pedantry and much talking leave no time".[335]

Liebig concluded by urging his fellow chemists to join the cause, and I suggest that this conclusion together with his identification of St Petersburg as a site of useful chemical research indicates a conciliatory attitude towards his "distinguished friend" Hess. Liebig would "rejoice to hear that blunders were made among us; for blunders are a proof that we are working". Instead, the main target of Liebig's attack was other German chemists, particularly those in Berlin.[336] The errors inherent in an "imperfect method" could be avoided by "a strict superintendence, which is soon spontaneously and mutually established", Liebig claimed, whereas doomed attempts to remove errors "deter from research; and their injurious influences on the development of organic chemistry will be long felt." Liebig's message was clear – my way is the only way to make progress with organic chemistry – as was his frustration at the lack of support from other German chemists. Ever ambitious, Liebig suspected that this outburst was unlikely to enhance his standing in Germany and he ended somewhat ruefully: "Truly if this were a matter of personal interest, it were folly to have said so much."[337]

In fact, Liebig was to say a lot more. Hess was a relative newcomer to organic analysis, having published mainly in the area of mineral analysis until about 1836,

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[335] Gregory did not name the cities – a rare deviation from Liebig's original.
[336] Liebig's criticisms were probably directed at Mitscherlich, with whom Liebig had fallen out very badly by this time, partly as a result of Mitscherlich's continued modifications of Liebig's analytical apparatus (described more fully in Chapter Four).
[337] Liebig's footnote to Hess (1838, 192) in Gregory's translation, Liebig 1839b, 30. Emphasis in original. Gregory replaced Paris and St Petersburg by France and Russia in his translation.

but he chose to pursue his challenge to Liebig's method of analysis and the work emerging from the Giessen laboratory.[338] One of Hess's contributions to organic chemistry was an analysis of saccharic acid (*Zuckersäure*), published in 1838.[339] Liebig's student the Norwegian M. C. J. Thaulow followed up on Hess's work, leading Hess to publish a second paper in the *Bulletin of the St Petersburg Academy* on the constitution of saccharic acid in which he not only disputed Thaulow's conclusions, but accused Thaulow of suppressing those results which did not support the expected outcome.[340] Liebig responded immediately and vigorously, reprinting Hess's article in the *Annalen der Pharmacie* and following it with a lengthy refutation in which he defended Thaulow's work, dissected every element of Hess's experimental work and turned Hess's accusations of unscientific practice against him. Whereas Hess's work had not even attempted to explain "where [saccharic acid] came from and what its relatives were", this "all-important question" was exactly what Thaulow had investigated and answered. Analysing a substance like saccharic acid was easy, the problem was "to make it speak". It was in St Petersburg rather than Giessen that the "well-known principle of avoiding anything which might instil doubt" was adhered to, and Liebig assured Hess that "this principle is looked upon by everyone in the laboratories here [in Giessen] as highly damaging and reprehensible, since therein lies the foundation of the ruin of all true scientific research".[341]

Hess's accusations indicate that he had intimate knowledge of laboratory practice in Giessen. Hess himself had not spent time in Giessen but one of his students at the Chief Pedagogical Institute in St Petersburg Woskresensky had recently matriculated in Chemistry in Giessen, where he had been a contemporary of Thaulow's.[342] We know that Woskresensky had at least some knowledge of Thaulow's analytical ability since he reported an analysis of quinic acid performed by Thaulow in corroboration of his own published results, rather as Blanchet and Sell had done some six years earlier.[343] There is no conclusive evidence to show that Woskresensky passed on detailed information to Hess about the way research was conducted in Giessen. Nevertheless, it is noteworthy that Woskresensky, who was regarded by Liebig as significantly more talented than his colleague Thaulow, did

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[338] Biographical information on Hess is taken from Leicester 1951; and Leicester 1972.
[339] Hess 1838.
[340] Hess 1839, 310.
[341] Liebig 1839a, 314 and 318-9.
[342] Fruton (1988, 58) reported that Woskresensky matriculated in 1837.
[343] Woskresensky 1839, 261.

not achieve a career in chemical research.[344] He published little beyond the three papers resulting from his time in Giessen, spending the majority of his time teaching in his capacity as Professor of Chemistry in St Petersburg.[345] This may, of course, have been the result of personal choice or force of circumstances, but it is tempting to speculate that Woskresensky forfeited Liebig's support because of his involvement in the Hess affair. If true, this would certainly have made it almost impossible for Woskresensky to pursue a career within the German chemical community, a path otherwise open to someone of his talents.[346]

In 1840, in a much less well-known epilogue to this exchange, Hess published a correction to his earlier work on saccharic acid. He admitted the existence of some printing errors but nevertheless asserted that Liebig had misconstrued his results.[347] This elicited a blistering response form Liebig. Hess, as far as Liebig was concerned, had completely missed the point. Liebig was adamant that the "true value of a chemical investigation does not consist of discovering numerical results and placing them next to one another". What mattered was that "these figures imply a mental concept" and that this concept should fit observed chemical behaviour as closely as possible.[348] Liebig insisted that the interpretation of analytical results in terms of chemical constitution and transformation was the true goal of scientific investigation, and that it was only possible to judge the value of analytical results in relation to such an interpretation. "If Thaulow's explanation is right," Liebig continued, "then his analyses are true; if it is false, then his analyses may nevertheless be reliable, but they require a different interpretation."[349] Experiment without theory could not produce useful chemical knowledge: "The correctness of a number depends on chance occurrences, the discovery of the truth which arises from it, is the task of science, but it will not be found using copper oxide, spirit lamps and oxygen gas alone".[350] In Liebig's view, only a poor chemist would become preoccupied with the technicalities of analysis at the expense of its scientific

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[344] Liebig (1839a, 314) referred to the "care and conscientiousness" with which Thaulow had carried out his investigations of Zuckersäure. Berzelius' letter to Liebig, 14 August 1838, in Lewicki (1991, 174) also thanked Liebig for all he had done for Thaulow, whom Berzelius hoped would become a chemist, even though his brain was not penetrating. On Woskresensky, see Liebig's footnote to Woskresensky 1839, 257.
[345] See also Woskresensky 1838a and 1838b. Fruton (1988, 58) included a short biography of Woskresensky (Voskressenski) according to which "[a]part from a useful paper on theobromine (1841), he published little afterward".
[346] See Gordin (2005) on chemical links between Germany and St Petersburg in this period.
[347] Hess 1840.
[348] Liebig 1840b, 118. Liebig (1837a, 13) had already expressed a very similar opinion.
[349] Liebig 1840b, 121-2.
[350] Ibid., 121.

meaning. "The worse the chemist, then, the sharper the evidence!!" he concluded in exasperation: Hess was no more than a "dilettante", working far outside the community of scientific chemists.[351]

Hess's attack on Giessen laboratory practice identified him as an outsider. Those trained in Giessen understood that it was essential to select results for publication and to interpret those selected results in the light of vast empirical experience. But in the eyes of a chemist elsewhere such judgements could easily appear unnecessary or unwarranted, perhaps even to have been motivated by a too strong desire to produce experimental evidence in support of a favoured theory. This view is confirmed by Liebig's earlier dispute with Zeise. Like Hess, Zeise used analytical results to challenge Liebig's publicly expressed beliefs, and Liebig responded with a strong defence of the analyst's reliance on skill and experience. Giessen analytical practice involved discarding poor analytical results, but the criteria applied by the analyst in making those decisions were nevertheless firmly rooted in sound experimental practice. Theory certainly played a role in the chemist's interpretation of analytical data, but this did not extend to deciding whether particular results were valid.

In 1837 Zeise's published analyses of a new substance led him to disagree with Berzelius' theory regarding the constitution of an important class of organic compounds then called ethers.[352] This was a topic of considerable interest to Liebig. He was keen to quash resistance to Berzelius' ideas and responded strongly to Zeise in order to silence others who might be tempted to agree with him.[353] Zeise's selection of the explanation that best agreed with his own opinions was, Liebig wrote, "not the course of chemistry today".[354] According to Liebig, since Zeise had not investigated his compound's decomposition products by analysis and therefore lacked information about its chemical transformations, he could only hypothesize about its composition and constitution. Moreover, although Zeise's published analytical data looked reasonable, Liebig did not consider that they supported the formula Zeise had suggested.[355] In particular, Zeise's determination of hydrogen was somewhat lower than his formula required, whereas - in line with the advice Liebig had provided in his *Introduction* (discussed in the previous section) – it was

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[351] Ibid., 123-4.
[352] Zeise 1837. Zeise was the Professor of Chemistry in Copenhagen. This unusual substance became known as Zeise's salt. Klein (2003, 180-184) explores the theoretical significance of Liebig's dispute with Zeise.
[353] Liebig to Berzelius, 21 December 1837, in Lewicki 1991, 140.
[354] Liebig 1837a, 13.
[355] Zeise's formula is accepted by chemists today.

well known to anyone who bothered to study the "hundreds of organic analyses from the most varied chemists" that the experimentally determined hydrogen content was always slightly higher than the theoretical composition required.[356]

Liebig also commented on the large variation in Zeise's results for hydrogen, from which he concluded that Zeise's analyses were untrustworthy. Liebig inferred that Zeise had given the results of all his attempted analyses, "even those whose correctness one might have reason to doubt", with the result that he had included "those hydrogen determinations that far exceeded his theoretical formula".[357] For Liebig, such adherence to "truthfulness and sincerity" was misguided because it obscured the main point of the research, which was not the execution and description of analyses but the investigation of chemical phenomena and transformations.[358] It was the duty of the chemist to present only trustworthy results, to "separate the wheat from the chaff", as "only the analyst himself can". As Liebig advised Zeise, "if some kind of error has occurred during the operation, then he [the analyst] must discard the result".[359]

Zeise's analyses certainly failed to meet Liebig's standards for consistency perhaps, as Liebig's comments suggest, because he had ignored indications that some of them were flawed. As I discussed in Chapter One, Blanchet and Sell took it in turns to repeat analyses until they obtained consistent results. It seems to have been common for Liebig's students to confirm each other's results – as Thaulow's analysis of chinic acid did for Woskresensky – a practice I would like to call collaborative replication. Similarly, both Liebig and his students selected results prior to publication, presumably according to experience gained during the performance of the analysis. For example, Oppermann reported only "the most successful" of his attempts to analyse oil of turpentine.[360] I showed earlier in this chapter that Liebig exercised exactly this kind of judgement in selecting results for publication. Usselman *et al.*'s reconstructed analyses, moreover, indicated that such selection was made easier because "features of the Liebig method itself tend to make plain which runs are good ones".[361] Giessen chemists understood that it

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[356] Liebig (1837a, 16) was a reference to the constant error of between 0.2 and 0.23 % in hydrogen determination identified by Wöhler and Liebig (1837, 13).
[357] Liebig 1837a, 18-19.
[358] This wording is from Liebig (1840a, 118) but the sentiment was often expressed in Liebig's publications throughout this period.
[359] Liebig 1837a, 19.
[360] Oppermann 1831a, 197.
[361] Usselman *et al.* 2005, 45.

was essential to use skill and judgement in deciding which results to publish, and that such decisions were part of sound experimental practice.

Zeise's method of obtaining a formula from his analytical data met with severe criticism from Liebig, partly because he ignored important collective experience gained from very large numbers of analyses and partly because he had relied on inadequate experimental evidence concerning the chemical behaviour of the substance under investigation. Determining formula required considering the results of analysis in an extensive context of empirical analytical experience, and other experimental and theoretical chemical knowledge. The *choice* of trustworthy results using information only available to the person who had actually carried out the experiment was not the same thing as the *suppression* of results because they did not support a favoured hypothesis but Zeise's criticism – like Hess's – shows that the two were not always easy to distinguish. These two chemists' exposure of the private practice of chemists in Liebig's laboratory invited others to form similarly unfavourable judgements, and Liebig was compelled to a swift and strongly worded denial and a sturdy defence of Giessen chemistry as "true scientific research". Maintaining confidence in the work of his research group was vital to Liebig's larger ambitions for organic chemistry and he therefore devoted considerable effort to managing the interface between his laboratory and the outside world.[362] The development of such skills, moreover, became a key component of training in Giessen with the result that those within Liebig's research school attained insider status from which others, such as Hess and Zeise, were excluded.

These episodes indicate that only those inside the Giessen laboratory learnt the full range of skills and practices needed to implement Liebig's approach to research at a time when the determination of organic formulae exceeded the limits of experimental accuracy. Even in the case of relatively simple substances, whose elemental composition could be safely deduced from analytical data, that composition could only be interpreted in constitutional terms by referring to a context of chemical transformations. Large numbers of analyses of a single substance were necessary to obtain convergent numerical results, but these results only acquired meaning through skilful negotiation between experimental outcome and theoretical interpretation. Because of this, training for research in Liebig's laboratory extended

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[362] Liebig was by no means the first person to consider this important. Shapiro (2003, 61) suggested that Newton had presented his experimental observations on optics "as unambiguously agreeing with experimental laws" in a "quest to establish a more certain science".

well beyond its usually accepted scope, encompassing a great deal more than how to perform analyses using the *Kaliapparat*. Students in Giessen learnt to understand what constituted a valid research problem, how to produce relevant and meaningful experimental results, and how to present their research in relation to contemporary chemical thinking. I contend that this is what Hofmann meant by "the art of carrying out experimental enquiries", which he clearly regarded as the most significant aspect of his own training in Giessen.[363]

## Conclusion

Neither Liebig's introduction of the *Kaliapparat* nor his development of a research school in Giessen were, in themselves, transforming events. The relationship between these two, moreover, is certainly not one of simple cause and effect. I have argued that Liebig's role in the development of nineteenth-century organic chemistry extended well beyond the introduction of a new technique of carbon determination and a new pedagogical system to encompass a novel, large-scale approach to chemical research and its publication. In sharp contrast to existing histories of Liebig's contribution to organic analysis, I have shown that it took years of work to stabilise the Giessen approach to analysis and that this approach was not easily disseminated to the wider chemical community. Even the empirically stabilised approach to organic analysis Liebig described in his 1837 *Introduction* did not reduce the assignment of a formula for an organic substance to a simple numerical deduction from the raw results of analysis, with the result that such formulae were often disputed.[364] Gaining acceptance for a particular formula depended on a variety of factors including the trust of the scientific community. Liebig used a range of strategies to build and maintain that trust, taking careful note of the distinction between the private and public arenas of science. He guided the research of those inside the Giessen laboratory, teaching them which results were worthy of publication and how to use those results in the production of formulae, and he was a tireless advocate for the scientific credentials of their work in the chemical community at large. Training for research in Giessen was not restricted to the application of experimental techniques to research problems selected by the director, but included managing the interface between the laboratory and the outside world

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[363] Hofmann 1871a, 146.

[364] Advances in technique and instrumentation during the 1840s removed much of the need for skill and judgement in producing a formula from analytical data, so that the 2nd edition of Liebig's *Introduction* (1853) could describe this process in terms of simple numerical deduction.

It is not easy for us to understand how Liebig and his students were able to increase their knowledge of chemical phenomena and transformations at a time when merely knowing the elemental composition of a substance was frequently beyond their technical reach. Initially, like Hess and Zeise, we might be tempted to dismiss the methods of data handling and interpretation in Liebig's laboratory as exemplifying poor experimental practice. A similar response is detectable in the discomfort of Earman and Glymour and, to a lesser extent, Holton when contemplating the behaviour of Eddington and Millikan – both of whom made claims at least as controversial as any of Liebig's. Holton recognised the importance of experimental expertise acquired through long hours of painstaking repetition, made visible in the fact that Millikan "knew a good run when he saw one", but because Millikan did not explain this skill Holton remained uneasy with this aspect of Millikan's laboratory practice.[365] Earman and Glymour, meanwhile, interpreted Eddington's selection of data as threatening the scientific validity of his conclusions.[366] This study of organic analysis, on the contrary, shows that dealing with uncertainty was an *essential* aspect of cutting edge scientific research in Giessen. As Liebig explained to Hess, "avoiding anything which might instil doubt" was "the foundation of the ruin of all true scientific research".[367]

How did chemists in Liebig's laboratory learn to manage the inherent uncertainties in the practice of organic analysis during the 1830s and 40s? And what does this tell us about the production of scientific knowledge? For one thing, as Liebig's own writings and Usselman *et al.*'s reconstructed analyses show, Giessen chemists learnt to recognise in the context of many analyses whether the *Kaliapparat* was working properly or not – behaviour which, as Usselman *et al.* noted, should no longer be viewed as atypical and certainly ought not to be considered "dishonest or sloppy".[368] Scientists frequently have to make judgements about the relative value of experimental data, and we should understand this as a skilful practice needed to produce reliable knowledge about the world.

Second, although chemists worked hard in Giessen to produce new facts, they did not achieve this only by repeated analysis using the *Kaliapparat*. As Blanchet and Sell explained, replication – initially by one individual and later within the research group – played an important role in minimising errors, but only to within the limits of

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[365] Holton 1978a, 53.
[366] Earman and Glymour 1980, 85.
[367] Liebig 1839a, 314 and 318-319.
[368] Usselman *et al.* 2005, 45.

accuracy that affected formula. Even then, analytical data only acquired meaning in a broader context of additional experimental data, and theories of chemical constitution and transformation. Because of this, consensus about the results of analysis was not achieved across the wider scientific community by simple processes of replication and refutation. Useful chemical knowledge was produced in Giessen by collective investigations which depended on a delicate accommodation between theory and practice. And because Liebig, unlike Milikan, both taught this *philosophy of practice* to young chemists in his laboratory and wished to disseminate it more widely, it was a recurring feature in his published papers.

In essence, Liebig's approach depended on gathering a large amount of experimental evidence concerning the chemical nature of a substance and its decomposition products, including but by no means restricted to the results of quantitative analysis using the *Kaliapparat*. Interpreting this data – which had often been acquired through collective work – required the chemist to make a careful assessment of the relative certainty of each item of information and to construct the most plausible solution. The role of experimental data in this philosophy of practice was not to determine the outcome. Instead, the chemist proposed a theoretically reasonable formula which was neither contradicted nor made unlikely by any of the available data. This depiction of laboratory practice at the cutting edge may be controversial. It undoubtedly challenges traditional notions of the decisive role of experiment in the production of scientific knowledge, but I do not mean to imply that the reliance of Giessen chemists on selection, interpretation and inference makes their behaviour anything less than profoundly scientific. On the contrary, the nature of such judgements and the processes by which communities of scientists acquire, develop, and propagate the skills needed to make them seem to me to be important and largely poorly understood aspects of how science works.

By the late 1830s Liebig's faith in the analytical approach to research in organic chemistry was beginning to waver, and from the early 1840s his own research was mainly concerned with agricultural chemistry and physiology. This move has previously been interpreted as a disillusioned abandonment of organic chemistry but I contend that it was entirely consistent with the stated goals of Liebig's research programme since at least the mid-1830s.[369] Liebig certainly abandoned the disputed field of constitutional theory around 1840, but the application of recently

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[369] See, for example, Holmes 1973, 344.

stabilised analytical techniques – especially for the determination of nitrogen – to investigating chemical transformations in living things was exactly the method of gaining "insight into the highly secretive processes of the nutrition etc. of the animal organism" he had recommended in 1834.[370] The direction of Liebig's research during the 1840s appears discontinuous only when viewed from the standpoint of the practice of constructive organic synthesis which came to dominate chemistry in the late-nineteenth century. Seen from this perspective, constructive synthesis appears always to have been the ultimate goal of organic chemistry, whilst the application of organic analysis to agriculture and physiology was merely a diversion from that inevitable path. The following two chapters further undermine that view by showing that the primary purpose of early synthetic organic chemistry was analytical, and that it took almost fifty years for constructive synthesis to become the dominant practice of organic chemistry.

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[370] Liebig 1834g, 3.

# Chapter Three: Analysis, Identity and Transformation in the development of Organic Synthesis

> *[T]he aid of synthetical chemistry is required in every direction in arriving at a clear understanding of structure and of change.*
>
> *Emil Fischer (1907)*[371]

## Introduction

Synthetic organic chemists are conscious of their disciplinary history. Textbooks commonly date the birth of synthesis – and the sudden death of belief in a vital force – to 1828, the year in which Friedrich Wöhler produced urea by heating ammonium cyanate. William Perkin's creation of the artificial dye mauveine during his Easter vacation from the Royal College of Chemistry in 1856 is another well-known milestone, usually portrayed as marking the origin of the synthetic dye industry. And if you ask who is the greatest synthetic organic chemist you are likely to hear the name Emil Fischer. Most historians of science know Fischer – if they know him at all – as a carbohydrate chemist and Professor of Chemistry in the University of Berlin around 1900, but to organic chemists his syntheses and conformational analysis of sugars during the 1890s remain a supreme achievement in the elucidation of chemical structure without the aid of late twentieth-century techniques of instrumental analysis.

Fischer's structural and synthetical investigations of sugars were also recognised as epoch-making by his contemporaries. For the synthetic chemist Carl Graebe, for example, these "enormously successful" researches, together with the acceptance of "the doctrine of the position of atoms in space", defined a suitable endpoint for his 1920 *History of Organic Chemistry*. Yet despite the continuing centrality of such episodes in synthetic organic chemists' historical consciousness, Graebe's *History* remains the most recent comprehensive history of the discipline. Why is there so little subsequent historical writing concerning organic synthesis?[372] For one thing, the very existence of an apparently authoritative account written by a chemist who participated in the events described has led later historians of chemistry to focus on other areas. Because synthesis appeared always to have been the ultimate and inevitable goal of organic chemistry in his account, moreover, Graebe encouraged the belief that the development of organic synthesis did not require historical

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[371] Fischer 1928 [1907], 218.
[372] Russell 2004 is an exception, though it is worth noting that this essay was written primarily for practising organic chemists rather than historians of chemistry.

explanation. In this chapter, I challenge the assumption that organic chemists were always driven by the goal of constructive synthesis, and I do so partly by analysing the histories written by Graebe and other chemists.

Graebe devoted considerable effort to identifying examples of organic "syntheses" going back as far as Scheele's 1783 preparation of potassium cyanide, even though he conceded that these "had not been described as syntheses at that time, but as artificial formations or methods of preparation".[373] And although Graebe claimed to have described "the results of experimental and theoretical researches" theory generally determined practice in his account, which therefore gave the impression that synthetic chemistry had had little or no effect on the development of chemists' theoretical ideas.[374] J. R. Partington's later, highly influential four-volume *History of Chemistry* reinforced that message, dismissing organic synthesis in remarkably few pages.[375] Synthesis may have had important consequences for our understanding of biology, but it was of extremely limited theoretical, or indeed practical, significance within chemistry. Subsequent generations of historians of chemistry have largely followed Partington's lead, according organic synthesis a crucial role in the development of applied and industrial chemistry, and giving the impression that organic synthesis resulted from theoretical advances driven in other ways.[376]

The nature of the relationship between practice and theory in organic synthesis remains contentious today. The eminent synthetic chemist Gilbert Stork was outraged by a recent claim in the Royal Society of Chemistry's house journal that synthesis was now largely redundant since it was no longer the case that "the only way to be sure of compound's structure was to synthesise it".[377] Stork responded that an "important function" of natural product synthesis is "to elucidate the course of reactions in complex systems", thereby generating "many (most?) advances in [reaction] selectivity".[378] Stork's claim echoes the conclusion reached by Fischer almost exactly one hundred years earlier (see epigraph): according to both chemists, the process of organic synthesis plays an essential role in the development of

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[373] Graebe 1972 [1920], 54-57. Graebe's book, written "as a supplement to textbooks of organic chemistry", has never been translated into English, reflecting the fact that English-speaking organic chemists throughout the twentieth century were expected to have a working knowledge of German.
[374] Ibid., iii.
[375] Partington 1964, 259-260 (on Wöhler's synthesis of urea), 468-471 (on Berthelot's synthetic work), and 504-505 (on Kolbe).
[376] Mary Jo Nye's (1994) description of the emergence of theoretical chemistry from largely synthetical investigations of organic structure is a notable exception. See in particular Chapter 7 on the development of theoretical organic chemistry in Britain.
[377] Lowe 2007, 18.
[378] Stork 2007, 40.

chemical theories of structure and transformation. In other words, chemical theory must be connected to practice, and organic synthesis is not now and never has been *only* about the artificial preparation of the chosen target.

If the accounts of chemists and historians of chemistry – many of whom originally trained as chemists – are so at odds with one another on these issues, they have other substantial features in common. They tend to rob the term synthesis of its historical meanings, acknowledging only its modern, constructive sense, a lack of historicity which results in two contradictory approaches, both of which are frequently merged within a single account, as for example in Graebe's *History*. Organic synthesis, they claim, dates back to late-eighteenth century preparations of organic substances, but at the same time it only became possible once modern structural theories had become established in the late-nineteenth century. Such histories do not question the purpose of early syntheses nor ask when preparative goals became feasible and desirable because they assume that syntheses were always performed with the aim of producing pure organic compounds artificially. As a result, there has been almost no exploration of the *chemical* significance of organic synthesis and of the theoretical concepts and experimental skills and practices which made it possible to construct specific chemical targets by synthesis.

I have two major, complementary aims in this chapter, which I have therefore divided into two main sections. In the first, I re-examine those histories, including Graebe's and its late-nineteenth century predecessors, which have already served so extensively as source material for historians. Although, as I have indicated, historically insensitive readings have produced contradictory accounts with extremely limited explanatory power, the histories themselves nevertheless contain much of significance for our understanding of disciplinary formation in organic chemistry.[379] Their purpose was not to present a historically accurate version of events but to recast organic synthesis as an exact physical science whose practice might shed light on the very nature of life, and whose practitioners were developing powers over the material world of immense practical and economic significance. Once read in this light they reveal elements of a new history of synthetic organic chemistry in which both the causes and the purposes of synthesis are recoverable.

In section two I argue against the theoretical insignificance of organic synthesis by showing that the practice of synthesis contributed greatly to chemists' developing

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[379] These sources have been used, though with very different purposes in mind, by both Russell (1988) and Rocke (1994).

conceptions of constitution and reactivity, these new theoretical ideas in their turn encouraging chemists to attempt the construction of a range of natural organic substances. I claim that *synthetical experiments* performed by Liebig's most famous pupil August Hofmann were an attempt to break the deadlock reached by Liebig's analytical research programme around 1840. I explain how Hofmann's synthetical approach developed from the Giessen method of analysis and I argue that the constitutional analysis and artificial preparation of natural alkaloids were the ultimate targets of this work. Hofmann's synthetic research may generally be considered to have focused on the chemistry of artificial amines but I argue that he used compounds such as aniline as experimentally more tractable models for the natural alkaloids. I propose that these fascinating compounds were hugely influential in the development of organic chemistry in the nineteenth century, and I use a case study of the hemlock alkaloid coniine spanning two chapters to illustrate the importance of synthesis in the elucidation of constitution, and the insufficiency of constitutional knowledge in achieving synthesis. In this chapter I describe how an early, failed attempt to synthesise coniine prompted Hofmann's interest in coniine, leading him to revise its formula, establish its constitution and attempt its synthesis. In the concluding part of this case study (in Chapter Four) I show how Hofmann's work was necessary, but by no means sufficient, to enable Albert Ladenburg's 1886 synthesis of coniine – the first synthesis of a naturally occurring alkaloid.

Hofmann's constitutional analysis of coniine depended on large-scale investigations of natural and artificial organic bases carried out in his Berlin laboratory and I argue that this body of work, focused around a repertoire of novel, exhaustively researched chemical transformations, was central to contemporary appreciation of Hofmann's chemistry. My account of Hofmann's research programme and its achievements not only improves our understanding of his success, it also helps to explain why Hofmann, despite his persistent interest in the natural alkaloids, did not succeed in synthesising coniine, nor any other natural alkaloid. Although Hofmann's synthetical approach was an immensely powerful method of constitutional analysis, it was not particularly effective in the constructive synthesis of specific natural targets, being much better suited to the production of new, artificial substances.

In more general terms, my description of the constitutional investigation and eventual synthesis of coniine instantiates the crucial and hitherto missing link between the analytical skills developed in Liebig's laboratory and the ability of organic chemists from the 1860s onwards to synthesise increasingly complex natural substances. It also demonstrates that synthetic organic chemistry – just like

analytic – depended on a *philosophy of practice* aimed at managing uncertainty. Organic synthesis has usually been portrayed as the exercise of relatively routine constructive power based on mature structural understanding, but I show that this highly skilful practice depended on a finely balanced experimental strategy in which standard chemical transformations were used to improve highly provisional constitutional knowledge. One might go so far as to say that if quantitative analysis using the *Kaliapparat* was "the one true reagent" for Liebig, then a well-understood chemical reaction performed the same function for Hofmann.

Understanding Hofmann's research programme in this way changes our view of the relationship between analysis and synthesis in nineteenth-century organic chemistry, and hence of the historiography most appropriate to this field. Whereas analysis and synthesis are usually considered to be separate, if not opposing, facets of organic chemistry, I argue that they remained inextricably intertwined in a single experimental practice during the mid-nineteenth century. Structural analysis and constructive synthesis, I contend, did not become entirely distinct practices of organic chemistry until the introduction of twentieth-century instrumental techniques of analysis.[380] The synthetical approach to constitutional analysis – developed by Hofmann and others – was, moreover, an essential precursor to the constructive synthesis of natural organic compounds pursued by a younger generation of chemists including Ladenburg. This modified objective, I argue in Chapter Four, demanded a novel investigative approach and some very different experimental skills from chemists, so that the development of constructive synthesis marks a significant and previously unobserved discontinuity in the practice of organic chemistry during the late-nineteenth century. Reconsidering the development of organic synthesis from this perspective has important consequences for our understanding of when chemists began to attempt organic synthesis and what they hoped to achieve, what the term synthesis meant to them, and how and why synthetic organic chemistry became the dominant chemical sub-discipline of the late-nineteenth century and much of the twentieth.

## Chemists' Histories and the Meaning of Synthesis

Synthesis has a wide variety of meanings in organic chemistry, as the chemist and historian Colin Russell has noted. Yet Russell's study made little attempt to historicise practitioners' use of the term, choosing instead to emphasise the distinctions to be made between the syntheses of natural and artificial substances,

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[380] Morris 2000; Reinhardt 2006.

and whether such syntheses proceeded "from the elements directly" – called *total synthesis* – or merely from simpler substances.[381] As a result, and rather like Graebe, Russell treated as syntheses a number of preparations of organic substances not so regarded by the chemists who made them.[382] In this section, I examine the use of the term synthesis in the context of organic chemistry during the nineteenth century. I show how its original meaning was modified by chemists' developing constructive capability and in response to their changing theories of chemical constitution and transformation. The redefinition of synthesis, moreover, resulted in a re-classification of known chemical transformations as syntheses without regard for the historical context of their original development, a practice which I suggest was encouraged by the emergence of total synthesis as the ultimate criterion of synthetic achievement.[383]

The generally accepted first use of the term synthesis in the context of organic chemistry was attributed by Graebe to Hermann Kolbe in 1845.[384] I want to draw attention to the fact that, of the *two* occurrences of *Synthese* in Kolbe's paper Graebe chose to mention only the *second*, which referred explicitly to "synthesis from the elements".[385] Here, in the conclusion to his paper, Kolbe – writing whilst lodging with Hofmann in London[386] – anticipated a time when:

> *Were it once possible to reduce acetic acid to alcohol and to obtain sugar and starch from the latter, we should clearly be in a position to construct these general components of the plant kingdom by so-called artificial means from their most distant constituents.*[387]

Right at the start of this paper, however, Kolbe argued that his investigation of organic acids produced by the action of chlorine on carbon disulphide (*Schwefelkohlenstoff*) was "perhaps not entirely without interest for the theory of copulated acids".[388] Because these acids had been "produced by synthesis from bodies of the simplest possible composition", instead of by the decomposition of more complex substances, there could be almost no doubt about their constitution and they could therefore "certainly be regarded as prototypes of the series of

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[381] Rocke (2001, 248) attributed the first use of "total synthesis" to Berthelot in 1857.
[382] Russell 1987, 169. As I discuss in relation to the synthesis of coniine, chemists' use of previous preparations to fill in the steps required to complete a total synthesis is partly responsible for their often ahistorical view of synthesis.
[383] See, for instance, organic chemists' continuing priority debate concerning the total synthesis of quinine, referred to later in this chapter.
[384] Graebe 1972 [1920], 148-149.
[385] Kolbe 1845, 186.
[386] Rocke 1993, 61-5.
[387] Ibid., 186.
[388] Kolbe 1845, 145.

organic acids".[389] The synthetic origin of these acids was primarily of importance to Kolbe because it reduced the level of constitutional uncertainty but because both Graebe and, later, Partington ignored this original and, I shall argue, crucial meaning of synthesis it has almost entirely vanished from the history of chemistry.[390]

Even stronger constitutional preoccupations are detectable in Hofmann and John Blyth's use of the word synthesis in their 1843 paper *On Styrole*. On heating the neutral organic oil called styrole, Hofmann and Blyth obtained a solid "vitreous mass" which they named "metastyrole". Having established that "this metamorphosis of styrole takes place without loss of or addition to any one of its elements, and solely through a change in the molecular structure of this body produced through the action of heat", they proceeded to make a thorough investigation of the transformation – which they discovered took place very rapidly when styrole was exposed to light – and, in true Giessen style, of the decomposition products of metastyrole. "Analysis as well as synthesis", they concluded, "has equally proved that styrole and [metastyrole] possess the same constitution per cent".[391] Hofmann and Blyth did not find that the two compounds were isomeric and, after assigning a formula of $C_{16}H_8$ to styrole and $C_{14}H_7$ to metastyrole, they came to no conclusion about how one was converted into the other.[392] Hofmann and Blyth were clearly *not* using synthesis to refer to production from the elements, or even from a simpler substance, which makes this single, isolated decision to use the term all the more interesting. Whereas Kolbe's use implied an interest in synthesis as both formation from the elements and as a means of obtaining constitutional certainty, Hofmann and Blyth's somewhat earlier use related only to the second, now forgotten meaning.

The histories written by Graebe and Partington were predicated on acceptance of Wöhler's 1828 preparation of urea from ammonium cyanate as the first recognised synthesis of an organic substance from an inorganic starting material, and consequently as a definitive moment both in the rejection of vitalism and in the development of synthetic chemistry. John Brooke has argued in his discussion of the unification of chemistry that Wöhler's preparation was important for its impact on theories of chemical constitution rather than synthesis, and that the doctrine of

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[389] Ibid., 145-146.
[390] Partington (1964, 259-260) referred to Kolbe's paper and to Graebe 1972 [1920], 148-9.
[391] Blyth and Hofmann 1843, 348 ff.
[392] Ibid., 353.

vitalism was a good deal more resilient than such accounts suggest. [393] I agree with Brooke, but whereas for him this was the starting point for a discussion of the philosophical significance of synthesis, I am much more interested in how this standard story came to be written, why it so dominates the history of organic chemistry and what it hides.

Wöhler's preparation of urea was significant because it demonstrated the production of a new substance without any accompanying change in elemental composition – exemplifying what Berzelius later termed *isomerism*.[394] Although it was soon invested with a different significance, his observation was important *then* because it prompted chemists to develop constitutional theories in order to explain the possibility of isomerism.[395] Such constitutional theories guided chemists in the production of formulae by quantitative organic analysis, but they in their turn also incorporated the insights gained from synthetical chemistry during the 1840s and 50s. Wöhler's preparation of urea was therefore of indirect but nonetheless essential significance for the development of synthesis, as a tool of both constitutional analysis and, ultimately, molecular construction. When chemists including Adolf Baeyer and Carl Schorlemmer sought to construct a history for their discipline half-a-century later, *this* was what they chose to emphasise. In so doing, they created an intra-disciplinary historical reconstruction which has been widely and uncritically accepted ever since. Even where the historical inaccuracy of such accounts has been noted – as in the case of Brooke's essay – this has not prompted further investigation of the early development of synthetic organic chemistry within academic contexts.[396]

Despite its use by Kolbe, Marcellin Berthelot and others during the 1840s and 50s, the term synthesis was not in widespread use until the mid-1860s.[397] Even then, it by no means displaced other terms including preparation (*Darstellung*) and formation (*Bildung*) which had long been used to describe the production of one organic substance from another, including cases in which the starting material was constitutionally simpler than the product. Synthesis also began to form part of the

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[393] Brooke 1971, 368-369.
[394] Berzelius 1832, 44-48. Berzelius introduced the term *isomerism* on p. 47.
[395] Hofmann (1850, 93) claimed that "speculations as to the mode in which the various constituents are grouped" in organic compounds had been "forced upon us" by isomerism.
[396] Brooke's (1971, 375) assertion that synthesis has been made overly important by Whig histories is, I think, a reference to standard accounts of the development of a scientifically-based synthetic dye industry.
[397] Graebe (1972 [1920], 200-202) described Berthelot's research in synthesis during the 1850s.

advanced chemical curriculum during the 1860s. Berthelot, for example, delivered a series of lectures on the general methods of organic synthesis at the *Collège de France* in 1864. These lectures, accompanied by demonstrations but not by a practical course,[398] presented the methods by which "one succeeded in forming the simplest organic compounds from elementary bodies". Berthelot certainly sought to convey an existing body of knowledge concerning the synthesis of various classes of organic compounds including acids, alcohols and hydrocarbons, but his lectures suggest that he placed much greater importance on making his students aware of the crucial role played by organic synthesis in reuniting the chemistry of organic and inorganic substances.[399]

According to Alan Rocke, the originality of Berthelot's programme, which had also formed the basis of his 1860 *Organic Chemistry founded on Synthesis*, derived mainly from its emphasis on total synthesis, which was in turn motivated by primarily taxonomic and philosophical concerns.[400] Rocke agreed with Berthelot's biographer Jean Jacques that synthesis for Berthelot was "a kind of intellectual exercise, marvellous and abstract".[401] Berthelot's *Organic Chemistry* may still "be regarded as one of the great classics of nineteenth-century scientific literature", but Rocke presented a persuasive argument for its rejection by contemporary organic chemists in Germany including Kekulé, Kolbe and Wöhler. German chemists were aggravated by Berthelot's "apparent attempt to usurp the entire field" of organic synthesis, and they regarded his arguments about the philosophical significance of synthesis as old-fashioned. Rocke explained Berthelot's attitude to organic synthesis in primarily philosophical terms, concluding that "the German organic-chemical style proved more fruitful than that of Berthelot" in large part because German organic chemists actually performed "the sort of active manipulations praised (but not practised) by Berthelot".[402] I agree that Berthelot's approach to organic synthesis contributed little to the practical development of the discipline – the yields from most of his syntheses were too low to be preparatively useful – and

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[398] According to Rocke (2001, 279) Adolphe Wurtz directed the only teaching laboratory for chemistry in Paris following the closure of Pelouze's laboratory school in 1857.
[399] Berthelot 1864, v (direct quotation) and see, for example, p. 16, on the role of synthesis in chemistry.
[400] Rocke 2001, 248-251. Berthelot 1860.
[401] Rocke (2001, 252) cited Jacques (1987, 77).
[402] Rocke 2001, 252-6.

so the remainder of this chapter examines the German style of organic chemistry which was both more pragmatic and more productive.[403]

Synthesis also featured heavily in a series of historical lectures delivered by a young *Privatdozent* Albert Ladenburg to chemistry students in Heidelberg towards the end of the same decade. Ladenburg's various references to significant syntheses as "interesting" and "beautiful" would have left his audience in no doubt concerning the importance of synthesis to the development of their discipline.[404] Ladenburg's lectures were "an attempt to follow the development of our ideas of to-day from those that were formerly current", which their author hoped would "furnish a useful contribution towards the history of the chief chemical facts and theories".[405] These goals proved more durable than the lectures themselves, which were very substantially revised and extended in three further editions until shortly before Ladenburg's death in 1911.[406] One major difference between the first and subsequent editions was the extent of the discussion of organic chemistry in general, and synthetic organic chemistry in particular. An almost entirely new "Lecture XIV" in the 1900 edition dealt, amongst other things, with the "Constitution of the Alkaloids" and "Syntheses".[407] Ladenburg claimed that the constitutional investigations he described had been "occasioned by the numerous cases of isomerism which meet the chemist at almost every step, and the existence of which seems to require some explanation". Despite the theory of valency, he continued, such an explanation:

> *chiefly depends upon the much more extensive experimental material at our disposal. And this material has, in great part, been obtained by the application of a method which, even although [sic] it has been recognised for a long time as a possible one, has only attained to pre-eminent importance within comparatively recent times. I refer to the method of synthesis, which is, moreover, in many cases, not merely a means to an end, but is itself the aim of the experiments.*[408]

Towards the end of the century, synthesis was frequently an end in itself. It had, however, started out as a method of addressing constitutional questions, such investigations having been performed despite the retrospective inadequacy of constitutional theories. As Ladenburg had explained in 1869:

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[403] Berthelot's work is hardly referred to in Elbs' (1889) and Lellmann's (1887) compendia of synthetically useful reactions.
[404] Ladenburg 1869b, 276 ("interessante") and 288 ("schöne").
[405] Ladenburg 1869b (v and vi) from the translation in Ladenburg 1900 (v and vi).
[406] These editions appeared, with virtually identical Forward, in 1887, 1902 and 1907 in the original German. An English translation of the 2nd edition was published in 1900 and later revised in 1905.
[407] Ladenburg 1900, 272.
[408] Ibid., 288.

> *It may appear remarkable to many persons, into whose hands a treatise on organic compounds published in the [eighteen-] twenties, or earlier, may chance to fall, that even at that time, when this department of chemistry was in so backward a state of development, experiments were made in order to obtain some information as to the constitution, or mode of arrangement of the atoms, of compounds. A pursuit of this kind may be regarded as idle speculation, and yet scientific chemistry was directed, at an early period, towards such considerations.*[409]

Ladenburg's lectures, despite their self-professed theoretical bias, tell us that early constitutional investigations hugely pre-dated what a late-nineteenth century organic chemist would recognise as a viable constitutional or structural theory, and that synthesis provided crucial experimental evidence about the "chemical nature" of substances at a time when such theories remained inadequate. Ladenburg expressed the hope that his book might "serve as a guide for those who may desire to engage their attention more particularly with special investigations in this department [chemical history]."[410] It certainly became a staple in the training of chemists across Western Europe during the late-nineteenth and early-twentieth centuries.[411] How was the theory-practice relationship to which Ladenburg drew such careful attention so completely obliterated from twentieth-century history of chemistry?

In July 1878 Baeyer, then Professor of Chemistry in Munich, delivered a lecture entitled *On Chemical Synthesis* to mark the birthday of King Ludwig II.[412] Baeyer presented a carefully-crafted image of a mature physical science founded on exact and well-understood laws: challenges remained, but all were solvable in principle. Baeyer wanted to show his audience, "how this science fruitfully penetrates all branches of human wisdom linked to matter, speculative philosophy, the science of life and the art of creating valuable industrial products".[413] He achieved this partly by revising the significance of events like Wöhler's preparation of urea, which he claimed had "opened the possibility of experimental research to prepare artificially the numberless materials of the plant and animal kingdoms, and perhaps also – even if only in the distant future – to solve the great puzzle which we call life".[414] Baeyer began by defining chemical synthesis as "a system of methods which have the goal of constructing more complicated compounds from simpler ones". This operational definition was quickly superseded, following Baeyer's exposition of the

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[409] Ladenburg (1869, 123) slightly adapted from the translation in Ladenburg 1900 (116-117).
[410] Ladenburg 1869, v, from the translation in Ladenburg 1900, v.
[411] Ladenburg's lectures were also translated into French. See Ladenburg 1911.
[412] Baeyer 1878.
[413] Ibid., 4.
[414] Ibid. Baeyer also attributed the re-unification of chemistry to Wöhler's urea synthesis.

atomic and structural theories on which synthesis depended, by a vision of synthetic chemistry as "building bigger [systems] from smaller and thereby acting as the architect, only that the attractive force of the atoms is used instead of mortar".[415]

This theoretical basis enabled Baeyer to discuss the progress of chemical reactions at the atomic level and to assert that even the synthesis of protein – a complex organic material – was "not a thing of impossibility".[416] Baeyer was also keen to promote the importance of synthesis to the German economy. Synthesis was important because plant and animal products could be produced cheaply and in large quantities. "The most shining example of this kind is alizarin," Baeyer claimed in somewhat immodest triumph, "whose artificial preparation was discovered in the year 1868 in my laboratory by Mr Graebe and Mr Liebermann."[417] In conclusion, Baeyer paid due respect to the "spiritual originator" of Germany's dominant chemical industry, "none other than Liebig, the man who made the German laboratory into the first in the world".[418]

Baeyer's speech exemplifies a number of extremely persistent elements in histories of organic synthesis, presumably because later historians have been tempted to believe that – because it was written by a chemist whose work centred on synthesis and recently after the events it described – it provided an accurate historical account. Baeyer's re-interpretation of Wöhler's urea synthesis ought, however, to awaken our suspicions. The production of natural and artificial dyes was certainly very important to the development of Germany's chemical industry during the late-nineteenth century but the development of organic synthesis was by no means as theoretically driven as Baeyer's account suggested. Equally, Baeyer's identification of Liebig's development of the laboratory with his role as founder of the German chemical industry provides an early instance of a widely-disseminated yet historically limited account of Liebig's greatness. There is, in particular, no suggestion of how the training of large numbers of young chemists in quantitative organic analysis could lead to, or even assist, the development of synthetic organic chemistry.

The first history devoted to organic chemistry appeared in the following year when Carl Schorlemmer, Professor of Organic Chemsitry at Owens College, Manchester, published *The Rise and Development of Organic Chemistry*.[419] Schorlemmer was

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[415] Ibid. See also p. 13.
[416] Ibid., 16 (on the chlorination of methane) and 20 (on the synthesis of protein).
[417] Ibid., 20.
[418] Ibid., 22.
[419] Schorlemmer 1879.

keen to claim an ancient legacy for what he called "our Science", whose history he too traced in essentially theoretical terms.[420] Schorlemmer devoted the last two chapters of his short book to organic synthesis, claiming in the opening of the first of these that "as soon as a clear insight into the constitution of organic bodies was gained, methods were found by means of which bodies hitherto formed only by the vital process could be built up from their elements".[421] This theoretically-determinist orientation did not, however, prevent him from spelling out the significance of synthetic work in resolving constitutional questions, as for example in the case of acetic acid.[422] Schorlemmer wanted to persuade readers of the scientific credentials of organic chemistry, but his own history shows how poorly organic chemistry fitted the accepted model of practice as driven by theory.

When listing early syntheses of organic bodies, mainly dating from the 1840s, Schorlemmer commented that "it was not till long afterwards that these reactions were recognised as syntheses". He continued by explaining one reason for that re-classification: "These examples show that by organic synthesis we understand not only the building up of compounds from the elements, but also the linking of carbon atoms".[423] By 1880, organic chemists were re-defining synthesis to reflect recently accepted structural conceptions of how chemical reactions proceeded, and they did not hesitate to apply these new definitions to earlier work. When Ladenburg claimed "the first total synthesis of an alkaloid" with his 1886 synthesis of coniine, for example, he drew upon 17 earlier papers beginning with Kolbe's 1845 preparation of acetic acid, only a small fraction of which were considered to describe synthetic processes at the time they were published.[424] Completing a formal total synthesis was an important motive for chemists' re-classification of earlier work and it was useful in establishing chemists' repertoire of transformations, but it also had the effect of disconnecting synthetic knowledge from its historical context. In making previous preparations part of contemporary syntheses, and of a contemporary body of knowledge, chemists encouraged the belief that such work *had always had* the significance with which they now invested it – with the consequences I have already discussed.

Managing this body of knowledge resulted in the publication of practical compendia of synthetically important organic reactions in Germany in the late 1880s and I

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[420] Arthur Smithells' "Preface" to Schorlemmer 1894, vi.
[421] Schorlemmer 1879, 98.
[422] Schorlemmer 1894, 120-122.
[423] Schorlemmer 1894, 198.
[424] Ladenburg 1886a and 1888a.

examine two of these to show that, although the definition of synthesis in terms of linking carbon atoms proved durable and ultimately dominant, it was not immediately and universally adopted. The first, Eugen Lellmann's 1887 *Principles of Organic Synthesis*, conceived synthesis as the "building-up of organic substances", emphasising the general applicability of what he termed "group reactions" and the level of certainty – or uncertainty – with which the constitutional progress and outcome of each reaction was known.[425] Lellmann, a *Privatdozent* at the University of Tübingen, wrote his book to help advanced students instruct themselves in "the methods of carbon chemistry", with a view to making their work in the preparative laboratory easier.[426]

This pedagogical motive was at least partly shared by Karl Elbs' slightly later book *The Synthetic Methods of Preparation of Carbon Compounds.*[427] Like Lellmann, Elbs included exhaustive references to the published literature, and he sought to provide beginners with a text of "practical utility". He was clearly also irritated by chemists' decision "to write no more recipes", with the result that even experts had to waste time and effort rediscovering necessary practical details.[428] Elbs, then *Außerordentlicher Professor* at the University of Freiburg, probably anticipated that his comprehensive guide would be useful to experienced practitioners, as well as novices. By 1889, Elbs explained, "as soon as the preparation of a substance is necessary, one has the choice of different routes which lead to its construction from easily obtainable starting materials". Elbs recognised the highly variable meaning of the term synthesis, which he asserted was then most widely interpreted as the preparation of more complicated substances from less, although it could also refer to obtaining naturally occurring chemical compounds by artificial means. Like Baeyer, Elbs chose to include under synthesis "such chemical methods of formation of carbon compounds whereby carbon atoms, which were previously not at all or not directly bonded together, become bonded" and, like Schorlemmer, he gave this newer, narrower, structurally based definition of synthesis precedence over all others.[429]

Elbs included a short history of organic synthesis in the introduction to his book. As Baeyer and Schorlemmer had done before him, Elbs portrayed Wöhler's preparation

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[425] Lellmann 1887. See "Einleitung": 1 ("Aufbau organischer Substanzen" and "Gruppenreactionen"), and "Vorrede": iv ("wünschenswerthen Sicherheit", "Unsicherheit").
[426] Lellmann 1887, iii.
[427] Elbs 1889.
[428] Ibid., iii-iv.
[429] Ibid., 2.

of urea as a synthesis, an isolated achievement in the quest to produce more complicated compounds from simpler ones. At this point, however, Elbs' account diverged markedly from these earlier histories. He claimed that it was only in the late 1840s that "one began to appreciate the value of synthetical methods of formation for the knowledge of the chemical nature of compounds". Then, once the "atomic construction" of the major classes of carbon compounds was known, together with "reliable clues ... on which synthetical experiments could be based", synthetic methods had developed "extraordinarily quickly", together with a huge body of experimental results which Elbs declared to be of "great theoretical and practical significance".[430] In Elbs' account, as in Ladenburg's, experiment and theory were presented as intimately inter-connected at all points in the development of synthesis, whose value ultimately encompassed both.

I have drawn attention to differences between the histories written by Ladenburg and Elbs, and those of Baeyer and Schorlemmer. Whereas pedagogical texts like Elbs' and Ladenburg's were intended for a community of practising chemists who either already understood, or were in the process of learning, how theory and experiment were linked in the research laboratory, histories written for a broader audience – for what Baeyer termed "the laity" – had other jobs to do.[431] Texts intended for practitioners of the discipline had to represent chemistry in recognisable ways, but it was much more important that accounts of scientific production for public consumption established organic chemistry as a well-understood, theory-driven science of great economic importance. Synthetic organic chemistry might be the dominant chemical sub-discipline, widely accepted as providing the most effective basic training even for would-be physical chemists, but the rapid growth in student numbers and new experimental practices meant that it was also one of the most expensive sciences.[432] The highly successful German dye industry was a major if often indirect source of funding for the huge luxuriously equipped institutes for organic chemistry then found throughout Germany but organic chemistry was nevertheless competing with other disciplines for limited financial resources.[433]

These considerations have important implications for our approach to the history of organic synthesis. For one thing, we should be aware that when nineteenth-century

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[430] Ibid., 1.
[431] Baeyer 1878, 4.
[432] See Ostwald (1898, 7) on the importance of organic "preparative exercises" for the training of physical chemists.
[433] See Baeyer (1878, 20-22) on the contribution of synthetic alizarin. Travis (1993) described the role of the German dye industry in funding organic chemistry.

organic chemists referred to existing or prospective practical benefits of the synthetic preparation of organic substances this was probably at least partly motivated by a desire to make their new and expensive discipline appear worthy of support. Similarly, when writing the history of their discipline in the late-nineteenth century, organic chemists were often consciously re-shaping its early intellectual foundations in keeping with its impressive achievements and recently elevated status. Such histories can still be useful, for example to provide evidence concerning disciplinary self-image, but their uncritical use as accurate historical sources has had doubly unfortunate consequences for the history of organic chemistry. Our present persistently a-historical view of the development of synthetic organic chemistry originates with these apparently authoritative histories, and their existence has effectively diverted historians away from this area since the early-twentieth century.

The meaning of "synthesis" changed substantially between 1840 and 1890 as chemists adopted an increasingly specific definition expressed in relation to links between atoms in preference to the earlier sense of "building up". The high degree of constitutional uncertainty associated with synthesis as "building up" was becoming a thing of the past, thanks to the mass of data produced by *synthetical experiments*. Chemists, mainly in Germany, used that data as the foundation for novel theories of constitution, reactivity and – eventually – structure, and they began to perceive synthesis in new ways as a result. The redefinition of synthesis took account of improved constitutional knowledge, derived from synthesis as well as analysis, and it was much more helpful in interpreting and classifying the outcome of chemical reactions. This enhanced understanding of chemical transformation in relation to structure was crucial in enabling chemists to shift the goals of synthesis away from constitutional investigation and towards construction. Around the mid-century, however, analysis and synthesis in organic chemistry remained complementary processes incorporating a similar set of investigative tools - just as had long been the case in the inorganic realm. Only as its meaning and goals altered did organic synthesis diverge from analysis to become a sub-discipline in its own right, with its own specialised methods for the construction of organic substances of known composition and structure.

## Synthesis and Chemical Identity

> *Chemists at once brought a lively interest to bear on aniline and quinoline, since the hope seemed not unjustified that a careful study of these bases would either lead to the artificial preparation of the natural alkaloids or yet give important explanations of their nature. The synthesis of the vegetable alkaloids is, as is known, even today an only partly solved task; but the route thereto has been particularly levelled through Hofmann's work, and I need only remind you of his recent beautiful investigations of piperidine and coniine in order to prove, with what iron persistence the master has striven to follow this path to its goal, and how much of what has been achieved we owe to him.*
>
> *Ferdinand Tiemann (1892)*[434]

I argued in the preceding section that constitutional investigation was a major motive for early *synthetical experiments*. The concept of constitution – the arrangement or grouping of elements within the molecule – was introduced by chemists during the 1830s when they realised that a large number of distinct organic substances had extremely similar or even identical composition. As a result, determining the composition of an organic substance was insufficient to establish its identity, leading chemists to develop constitutional theories to account for the existence of isomers and the similar chemical behaviour of what they inferred were constitutionally similar substances. The notion of constitution, however, remained highly subjective throughout the mid-nineteenth century partly because of the lack of any agreement regarding the underlying points of reference for a constitutional theory and partly because the available experimental data did not effectively discriminate between competing theories. Chemists therefore continued to rely on traditional characteristics including chemical and physiological behaviour, appearance, crystal form, solubility, smell and taste to settle questions of identity. At the same time, I argue, they anticipated that additional experimental evidence produced by preparing a substance artificially would be useful in reducing constitutional uncertainty and hence in developing a new understanding of chemical identity.

In 1843, for example, a young August Hofmann struggled to explain the formation and determine the composition of a substance called chloranil which had been obtained by Otto Linné Erdmann by the action of chlorine on indigo. Hofmann "soon learnt that chloranil is often formed, as the last product of decomposition of organic bodies, under the united influence of oxygen and chlorine", and he was inspired by known behavioural analogy to attempt the preparation of chloranil from the hydrate of phenyle.[435] He was successful, and declared the substance he had produced to

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[434] Tiemann 1892, 3382-3383.
[435] Hofmann 1843b, 228-229.

be "identical" to Erdmann's chloranil on the basis of an extensive description of its physical and chemical properties. Similar impurities in his sample and Erdmann's meant that, although both their combustion analyses gave too high a percentage by mass of carbon, the results were nevertheless in good agreement with each other.[436] So far so good, but when Hofmann attempted to produce chloranil by boiling benzoic acid with hydrochloric acid and chlorate of potassa, he failed. He had expected this "metamorphosis" to occur with benzoic acid because it took place with salicylous acid. As he explained: "Although it is known that benzoic acid and salicylous acid are identical, still the former, when treated [in this way], does not yield chloranil."[437] In other words, one pair of supposedly "identical" chemical substances – benzoic and salicylous acids – reacted in completely dissimilar ways, whilst chemical behaviour and physical properties were used elsewhere (and in the absence of acceptable quantitative analytical data) to claim that two other substances – chloranil as prepared by Erdmann and by Hofmann – were "identical".

It is not my purpose here to investigate the validity of either of these particular claims in detail but this paper, the first of several Hofmann published concerning the action of chlorine and oxygen on organic bases obtained from coal tar, serves to illustrate how tenuous the concept of chemical identity remained in the 1840s. The re-conceptualisation around 1830 of plant substances as "purified carbon compounds" with fixed composition might appear to us to simplify the chemist's task, but working within this new ontology was very hard indeed.[438] Obtaining pure substances was difficult – quite often, as in the case of chloranil, it was impossible. Repeated re-crystallisation remained by far the most reliable method of purification but many substances, including many of the most interesting naturally occurring organic solids, could not be coaxed into crystalline form. There were, moreover, no accepted criteria by which purity could be assessed. Although melting point and boiling point were often reported for substances purified by crystallisation or distillation, these figures were not yet understood as reliable indicators of purity and identity (see Chapter Four). Mid-nineteenth century organic chemists placed far more weight on other physical, chemical and even physiological properties when attempting to decide what their experiments had produced.

A substance's chemical behaviour was central to determining its identity as well as estimating its purity, but the relationship between reactivity and constitution was not

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[436] Ibid., 229-230.
[437] Ibid., 232-233.
[438] Klein 2005, 261. See also pp. 313-320; and Klein and Lefèvre 2007, Chapter 16.

simple. Dissimilar reactivity usually implied different constitution – as in Hofmann and James Muspratt's 1845 comparison of nitrous ether and nitrobenzol – but the reverse was often not the case. For example, chlorine could be substituted for hydrogen without affecting a substance's "fundamental properties".[439] Whereas today a unique three-dimensional structure defines chemical identity, the concepts of constitution, reactivity and chemical identity were inseparable and interdependent in the thinking of mid-nineteenth century chemists. None acquired meaning without the others, a chemist's interpretation of each depending on his theoretical and experimental engagement with all three.

As Muspratt and Hofmann explained in 1843, the current impossibility of predicting the outcome of a chemical metamorphosis "lies in the deficiency of our present knowledge respecting the true constitution of organic bodies".[440] Equally, establishing the constitution of a substance depended on studying its decomposition to simpler substances of known constitution. How did chemists break out of this complex circularity? According to Muspratt and Hofmann, the kind of "analytical" researches they learned to carry out in Giessen "have made us better acquainted with the transformations which an organic substance suffers under the influence of the most different agents". This relatively secure understanding of chemical change, they believed, "qualified" them to attempt "synthetical experiments" and enabled them "to proceed in this direction with greater certainty".[441] Processes of chemical transformation, which had been the key to establishing chemical composition and constitution by analysis, now became crucial in enabling early attempts to synthesise organic substances, those attempts being primarily intended to confirm composition and constitution. In other words, the switch to synthesis was driven by the application of a growing body of reliable chemical transformations to the investigation of chemical constitution, that body of knowledge itself being derived from organic analysis as practised in Giessen. Such *synthetical experiments* not only shared their ultimate purpose with earlier analytical investigations but they depended on the same *philosophy of practice* for the management of unavoidable uncertainties.

This intimate connection between the Giessen method of organic analysis and the development of organic synthesis adds an entirely new dimension to Liebig's scientific legacy, and to the causes of Hofmann's rise to fame. Many histories of

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[439] Muspratt and Hofmann 1845, 113 and 114.
[440] Muspratt and Hofmann 1843a, 249.
[441] Muspratt and Hofmann 1843b, 367.

chemistry acknowledge that Hofmann played an important part in the development of organic synthesis, but they usually relate this either to his preparation of artificial dyestuffs or to his development of several reactions subsequently found to be synthetically useful.[442] At the same time, although Hofmann's early research programme is well known to have centred on the constitutional investigation and preparation of artificial organic amines, this has been widely assumed to be a straightforward continuation of the investigation of the distillation products of coal tar which he had been directed by Liebig to undertake whilst a doctoral student in Giessen. I contend that these evaluations of Hofmann's contribution simultaneously underestimate both his debt to Liebig and the significance and originality of his own role in the development of synthetic organic chemistry. Whilst Hofmann was guided by Liebig to adopt a synthetical approach in order to break the deadlock reached by analytical organic chemistry around 1840, he subsequently developed and applied this research strategy to *artificial* organic bases with the explicit goal of understanding the constitution and reactivity of the *natural* alkaloids.

## The challenge of the alkaloids

I have shown in earlier chapters that producing reliable analytical data for the alkaloids was important in setting the course of Liebig's research during the late 1820s. By the late 1830s, however, Liebig was clear that his analytical approach *could not* resolve questions concerning the composition, much less the constitution, of the alkaloids. The available methods of organic analysis were not capable of resolving disputes about their hydrogen content and it was not possible, despite the analyses Liebig had published in 1831, to be sure about the connection between their composition and reactivity. Unable to pursue this line of research using the methods he had established at such great cost, I argue that Liebig believed synthetical investigations of artificial nitrogenous bases might provide insight into the constitution and reactivity of the natural alkaloids – and that he entrusted this task to the most outstanding young chemist then in Giessen, Hofmann. I therefore argue that Hofmann's research programme, though apparently largely concerned with artificial amines, was nevertheless ultimately directed towards understanding the natural alkaloids – whose remarkable physiological activity, reactivity and constitution were so significant in determining the direction of chemical research throughout the nineteenth century.

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[442] This is true of several essays in Meinel and Scholz 1992, but see also Brock 1992, 293-308.

The alkaloids were tempting subjects of investigation even though chemists soon learnt that they were compositionally and constitutionally complex. One important factor was that they could be obtained in fairly high levels of purity: their chemical basicity meant that they could be extracted relatively easily from the plant source, the impure base then being converted into a salt which could be crystallised.[443] Their widespread use in medicine also meant that alkaloids such as morphine were available to chemists in quite large amounts and – provided they were on friendly terms with a good pharmacist or apothecary – with relatively little effort.[444] The alkaloids, moreover, exerted a profound influence on the relationship between pharmaceutical chemistry and medicine: for the first time, chemists were able to provide medical practitioners with effective means of treatment and – in some cases – cure, and they were eager to extend this role. Whilst opium and laudanum exerted a powerful influence on the Victorian literary imagination, chemically pure alkaloids held out a tantalising promise to organic chemists.[445]

Advances in analytical techniques early in the nineteenth century had enabled European pharmacists to isolate new and curious substances from vegetable drugs. These substances, which intensified the medicinal properties of the drugs, were difficult to classify within existing chemical systems but were gradually shown to share important chemical properties. All reacted with acids to form salts and all contained nitrogen, leading to early speculation that they might be related to ammonia. This new class of substance, initially called "salifiable vegetable bases", soon became known as the vegetable alkaloids.[446] Pharmacists including Joseph Pelletier and Joseph Caventou, who isolated quinine from cinchona bark in 1820, examined many vegetable substances in the search for new members of the family, greatly increasing their number by 1870.[447]

Morphine and quinine in particular quickly became essential in medical practice, demand far out-stripping supply from their original sources, the opium poppy and the Peruvian cinchona tree. Quinine, which was the treatment of choice for tropical or intermittent fever (now known as malaria) by the 1840s, was expensive and often

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[443] See O'Shaughnessy (1844, 267) on the extraction of quinine from cinchona bark and its crystallisation as quinine sulphate.
[444] The family firm of Merck in Darmstadt, for example, continued to supply pure coniine to Hofmann, just as it had previously supplied morphine to Liebig. See Hofmann 1881c, 707.
[445] Compare the central role of opium in Wilkie Collins' (1986 [1868]) *The Moonstone* with Hofmann's (1871b, 9-10) emphasis on the importance of opium and quinine in medicine.
[446] Lesch 1981.
[447] Pelletier and Caventou 1820. Lesch (1981, 305) discussed the increase in number of alkaloids during this period.

simply unavailable where it was most needed. In Calcutta, for example, William O'Shaughnessy Assistant Surgeon in the Bengal Army and Professor of Chemistry and Medicine at the recently founded Medical College of Calcutta, provided extensive information about possible substitutes for quinine in his *Bengal Pharmacopoeia* of 1844.[448] One of these was anarcotine, an alkaloid found in large concentrations alongside morphine in the opium then being cultivated under government auspices in British Bengal.[449] Although, according to O'Shaughnessy, "we should recommend quinine in preference, because its qualities are proved, and the disease admits of no delay or trifling", where quinine was unavailable or too expensive "anarcotine may be boldly had recourse to".[450]

Quinine's expense also had a deleterious effect on its chemical investigation. As Hofmann explained in 1849, "A detailed investigation of the metamorphoses of the natural bases is greatly hindered by the costliness of the materials, but there is scarcely a field in organic chemistry the cultivation of which promises a richer harvest."[451] The richness of that harvest was literal as well as metaphorical. In 1843 Hofmann and Muspratt – pursuing a theme introduced several years earlier by Liebig and Wöhler[452] – explicitly anticipated the possibility of synthesising quinine. Although they declared that the "artificial production of bodies occurring in nature presents at first a purely theoretical interest", they quickly moved on to address the "practical importance" of such endeavours:

> *Of what influence would be the invention of a process for procuring the medicinal vegetable alkaloids in a simple artificial way? If a chemist should succeed in transforming in an easy manner* naphthaline *into* quinine, *we would justly revere him as one of the noblest benefactors of our race.*[453]

We know from Brock's account of what he called the *Quinine-Quinidine Conspiracy* that Liebig and Hofmann pursued other rather more self-interested approaches to improving the supply of febrifuge principles in Britain during the mid-1840s.[454] The motivation for attempting to produce medicinally useful alkaloids by artificial means

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[448] Gorman (1983 and 1971) described O'Shaughnessy's chemistry and his better-known work on the Indian telegraph system.
[449] O'Shaughnessy (1842, 336-7) claimed 6% anarcotine and 10% morphine in Patna Garden opium, which exceeded the concentrations of these active components in English muriate of morphia.
[450] O'Shaughnessy 1844, iv and 261.
[451] Hofmann 1849a, 173.
[452] From Brock (1997, 89) which cited Liebig and Wöhler (1837 and 1838). Liebig and Wöhler predicted that sugar, salicylin and morphine would be artificially produced.
[453] Muspratt and Hofmann 1843b, 367-368. Emphasis in original.
[454] Brock 1997, Chapter 5.

was undoubtedly financial as well as philanthropic, but what made chemists like Liebig and Hofmann believe they might succeed?

One answer is that the possibility of preparing any organic substance artificially was simply an article of faith for Liebig and his pupils. As Hofmann and Muspratt had commented of the potential conversion of naphthaline into quinine in 1843, "Such a transformation has not as yet succeeded, but this does in nowise show its impossibility."[455] To some extent that confidence derived from Liebig, Wöhler and Berzelius and the belief that the same laws must govern chemical combination in the organic as well as the inorganic realm.[456] This line of reasoning was used to considerable effect by Hofmann in his 1849 *Reports* from the Royal College of Chemistry (hereafter RCC). But these *Reports*, which were circulated to the RCC's benefactors, also suggest another reason for Hofmann's determination. Although they mainly consisted of reprints of published research papers introduced by Hofmann, the *Reports* began with a financial statement indicating the dire straits into which the new college had already fallen. Doing chemistry was expensive, and considerably more expensive than the RCC's benefactors seemed to realise. Offering the prospect of new, commercially useful products was a useful tactic in attempting to elicit the additional financial support the college so badly needed.

In his *Introduction to Researches*, Hofmann was at pains to justify the number of investigations of artificial amines, none of which had "as yet found their way into any of the various appliances of life".[457] He did so by reminding his readers "of some actual benefits which studies of a similar nature have conferred upon society", beginning with a number of achievements in inorganic chemistry including "the artificial reproduction of the *lapis lazuli*".[458] If such preparations were possible in the inorganic world, Hofmann argued, it must also be possible to prepare organic substances and he anticipated that "the study of organic metamorphoses" would enable "the artificial formation in the laboratory, of substances formerly generated by direct vital processes exclusively".[459] Chemists' ability to form acetic acid "by combining its very elements", he asserted, was one of several facts which "encourage us to believe that ultimately we shall find chemical artifices by which we may arrange these same materials [carbonic acid, water, ammonia, sulphuric and

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[455] Muspratt and Hofmann 1843b, 368.
[456] Liebig and Wöhler 1837 and 1838; Berzelius 1815d, 275.
[457] Hofmann 1849b, LIV.
[458] Ibid., LV.
[459] Ibid., LVII.

phosphoric acids] into the various compounds elaborated by the processes of vitality".[460]

Yet Hofmann's focus was not so much the on the products as the processes of chemical transformation. In his opinion:

> *it is not the host of new substances, which we are continually discovering, that interest us so much, but new methods of operation, by which we may imitate ... the formative forces of nature. Every new reaction with which we become acquainted, is a step nearer to the solution of this grand problem.*[461]

Once again, Hofmann chose to illustrate his argument by referring to "the artificial formation of the natural alkaloids". "Everybody", he asserted, "must admit that the discovery of a simple process for preparing artificially the febrifuge principle of the Cinchona-bark, would confer a real blessing upon humanity", and he continued by claiming: "Now we have good grounds for the expectation that constructive Chemistry will not long remain without accomplishing this task."

What was the basis of Hofmann's optimism? "Already", he declared, "numerous substances have been artificially formed, which are in the closest relationship to quinine and cinchonine", the most striking of which was naphthalidine, a crystalline alkaloid formed from the hydrocarbon naphthaline which itself was produced in large quantities in the manufacture of coal-gas. By comparing the compositions of naphthalidine and quinine – though the latter was, according to Hofmann, "not finally ascertained" – Hofmann believed "it will be obvious that naphthalidine, differing only by the elements of two equivalents of water might pass into [quinine] simply by an assumption of water", although he did not expect it to be easy: "We cannot, of course, expect to induce the water to enter merely by placing it in contact; but a happy experimenter may attain this end by the discovery of an appropriate metamorphic process".[462] It must have appeared to Hofmann that his earlier proposal with Muspratt that quinine might be prepared from naphthaline had taken a significant step forward.

A minor modification of this idea lay behind Hofmann's encouragement in 1856 of the young William Perkin's attempts to make quinine by oxidation of allyltoluidine, which unexpectedly resulted in the formation of the artificial dyestuff Perkin called

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[460] Ibid., LIX-LX.
[461] Ibid., LX.
[462] Ibid., LXI.

*mauveine*.[463] Modern responses to Perkin's achievement are highly ambivalent: he is celebrated as the founder of the British dye industry, whilst at the same time being ridiculed for having attempted what is now understood to be an utterly implausible structural transformation.[464] In 1944, for example, the chemist Robert Burns Woodward – who had just claimed the total synthesis of quinine – asserted attempts to synthesise quinine had only become reasonable after its structure was elucidated in 1908. But a century earlier Hofmann believed it might be possible, and he was not alone. William Gregory – who had also studied with Liebig in Giessen – declared in 1852 that "if we can discover, as we probably shall, the true constitution of morphine and quinine, [...] we shall then have little difficulty in forming such bases".[465]

We now know that these hopes were destined to be disappointed: morphine and quinine were eventually synthesised during the mid-twentieth century by large teams of chemists with access to highly developed synthetic and analytical techniques.[466] A century earlier, however, there appeared to be good reasons for anticipating success. Hofmann's confidence was especially persistent, surviving until at least 1867 when, at his suggestion, the *Königliche preussische Akademie der Wissenschaften zu Berlin* announced a prize for the synthesis of any of the five vegetable alkaloids: quinine, cinchonine, strychnine, brucine, or morphine, all of which were in widespread medicinal use at the time. The Academy – presumably guided by Hofmann, who had been elected to membership following his return to Berlin in 1865 – "believed that the time has come for the solution of this task".[467] It was mistaken. When no answer was received by the original deadline of 1 March 1870, this was extended to 1 March 1873 and English added to the acceptable languages for submission (Latin, German and French) but this still failed to elicit any

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[463] Naphthalene ($C_{10}H_8$), naphthilidine ($C_{10}H_7NH_2$) and allyltoluidine ($C_9H_9NH_2$) have similar rational (molecular) formulae, though we now understand that the structure of allyltoluidine is quite different from the related structures of naphthalene and naphthilidine.

[464] In 1849 Hofmann took the composition of quinine to be $C_{20}H_{11}NO_2$, which (allowing for changes in atomic weights) is in good agreement with the modern $C_{20}H_{24}N_2O_2$.

[465] Gregory 1852, 3. As Meinel (1992, 36) has noted, Kolbe expressed a very similar opinion in 1858. See also, Berthelot 1860, Vol. II, p. 803.

[466] Quinine was first produced synthetically by Paul Rabe and Karl Kindler (1918). The Rabe-Kindler synthesis was crucial to Woodward and Doering's 1944 *total* synthesis of quinine. Stork *et al.* (2001) disputed the Rabe-Kindler synthesis, and hence the validity of Woodward's claim. For an extensive discussion of these debates, see Seeman 2007, and Smith and Williams 2008.

[467] The prize was recorded in the Preisschriften of the Academy for July 1867: Akademiearchiv, Berlin-Brandenburgische Akademie der Wissenschaften, Historische Abteilung, Abschnitt II: Akten der Preußischen Akademie der Wissenschaften 1812-1945, Signatur II-IX, 16, pp. 6-6R. It was also announced in *Berichte*, (1869) ii, 468-9.

credible claim to the prize of 100 Ducats.[468] The Academy did not mention the prize in 1873 or 1875, from which I infer that it attempted to minimise public embarrassment by silence.

The Academy and Hofmann were as mistaken about the feasibility of synthesising these alkaloids in 1867 as Hofmann and Perkin had been in attempting to produce quinine from allyltoluidine over ten years earlier, but we should be as wary of condemning one as the other. If Hofmann had good reasons for believing it was possible to prepare quinine artificially in 1856, this was still the case in 1867. Despite repeated failures nothing had occurred during that ten-year period to convince Hofmann that such attempts were bound to be unsuccessful. On the contrary, he had some grounds for thinking that the likelihood of success had increased. Understanding of the alkaloids had certainly improved: there was greater consensus about their elemental composition, even though their constitution remained largely intractable.[469] Hofmann's earlier uncertainty concerning the "form in which nitrogen is contained in an alkaloid" had largely been resolved by his introduction of the ammonia type and the classification of amines as primary, secondary or tertiary.[470] His relative security about the amine portion of the alkaloids was, moreover, reflected in the Academy's decision to offer its prize for the production of "a well characterised nitrogen-free compound" which could be converted into one of the alkaloids by the action of ammonia.[471]

Hofmann's optimism was partly the result of his own research focus on the amine portion even though, as the American chemist Albert Prescott commented in his 1887 lecture to the Chemical Section of the American Association for the Advancement of Science, "the type ammonia represents only the "ammonia rest," a small part of the molecule of a natural fixed alkaloid". According to Prescott, chemists had remained "[u]nable to reach a clew to the constitution of the larger

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[468] Preisschriften, Signatur II-IX, 16, p. 16. It is hard to place a modern financial value on this prize but I calculate that this weight of gold would be worth something in excess of $700,000 on today's money market.

[469] Hofmann (1849b, 173) declared himself "entirely ignorant" of the constitution of strychnine in 1849. The following year, Nicholson and Abel (1850, 242) reported that a "simple determination of the elements appeared to be of little assistance in the construction of the formula" of strychnine. Their analysis of strychnine and numerous of its salts led them to assign the formula $C_{42}H_{22}N_2O_4$, which differed slightly from *any* of the formulae previously proposed by Liebig, Regnault and Gerhardt, the only chemists to have analysed strychnine by 1850. The modern formula for strychnine is $C_{21}H_{22}N_2O_2$.

[470] Hofmann 1849a, 173.

[471] The possibility of awarding the prize for the synthesis of a nitrogen-free alkaloid precursor was also explained in *Berichte*, (1869) ii, 468-9.

part ... until within the past ten or fifteen years".[472] Even by the late 1880s, when the alkaloids had been classified into two families – one related to quinoline and the other to pyridine – constitutional knowledge of the alkaloids remained severely limited because these parent compounds were themselves so little understood.[473] Partial constitutional understanding was not, however, a deterrent to attempted synthesis. Hofmann had understood from the beginning that *synthetical experiments* might fail because of the limitations of current constitutional theories.[474] Where such experiments did not produce the desired end product – as in the case of Perkin's attempted synthesis of quinine, for example – they nevertheless had the potential to increase understanding of the substance's constitution or, more importantly in Hofmann's view, of the reaction by means of which the chemical transformation had been attempted.

Hofmann's development of a synthetical approach to organic chemistry relied on placing the reaction at the centre of his research strategy, and he was quick to apply these methods to the alkaloids. In 1843, whilst still in Giessen, Hofmann reported the outcome of an investigation of the reaction of quinine with chlorine he had carried out some time earlier. Unfortunately, he found that the products were hard to crystallise and therefore almost impossible to purify, analyse or characterise. As a result, and echoing a familiar Liebigian complaint, Hofmann regretted that the "properties of these substances are not well-defined, nor do their analyses bear the stamp of exactness, so that the science has gained but little by their execution".[475] Hofmann claimed that he had been prompted by these difficulties to investigate the production of chlorinated and brominated anilines.

According to this evidence, using artificial amines as a model for alkaloids was a pragmatic response to the numerous practical difficulties surrounding the investigation of the natural substances, but it also depended on a strong commitment to the chemical equivalence of natural and artificial substances. In the same year, Muspratt and Hofmann noted that the artificial bases bore "the greatest similarity with the natural ones in properties and composition", but that their simpler constitution and more manageable physical properties made them much more

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[472] Prescott 1887, 133.
[473] Gerhardt (1842) showed that quinoline was a decomposition product of both quinine and strychnine but chemists did not begin to understand the constitution of quinoline until the 1880s when Ladenburg identified the second family of pyridine alkaloids.
[474] Muspratt and Hofmann 1843b, 367.
[475] Hofmann 1843a, 268.

tractable experimental subjects.[476] Aniline in particular showed "properties and chemical character" closely resembling those of two natural alkaloids: nicotine obtained from tobacco leaves and coniine from the hemlock plant.[477] Hofmann's continuing research into aniline following his move to the RCC should therefore, I argue, be seen as the development and application of this strategy, the natural alkaloids remaining the ultimate target of this research. As Edward Nicholson one of Hofmann's first students explained in 1845:

> *It being a matter of indifference whether the base which I took for experiment was a natural alkaloid or one prepared artificially in the laboratory, I selected aniline, deeming it especially suited to my purpose, as this base generally forms with acids readily crystallizable compounds.*[478]

Hofmann's emphasis on the value of well-understood chemical transformations meant that the development of generally applicable methods of preparing artificial bases was another highly desirable goal but, notwithstanding their greater ease of handling, this was not easily achieved. "Basic bodies", Hofmann and Muspratt declared, "have further been produced by the action of ammonia upon organic bodies", yet these "modes [...] for the formation of organic bases are only applicable in a very few cases".[479] At that time, only Nikolai Zinin's method – the reduction of nitrated hydrocarbons using sulphuretted hydrogen – appeared to offer a more general solution, which Muspratt and Hofmann believed would "become of vast importance for the group of alkaloids", and they claimed that "if we could succeed in obtaining the [precursor] carbo-hydrogens [...] there would be no difficulty in procuring, in an artificial way, nicotine and coniine".[480]

I have shown that the natural alkaloids, especially those which – like morphine and quinine – were medicinally important, pervaded Hofmann's chemical thinking in the mid-nineteenth century. Yet despite their availability in pure, crystalline form, the alkaloids proved to be extremely challenging experimental subjects. Hofmann responded by developing a research programme incorporating two important, novel strategies, both of which he had learnt whilst in Liebig's Giessen laboratory. He applied synthetical rather than analytical techniques, and he used artificial amines to serve as experimentally simpler substitutes for the natural alkaloids. Hofmann's study of aniline in particular should be understood as a model for the naturally occurring alkaloids nicotine and coniine. Hofmann's work had well-known

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[476] Muspratt and Hofmann 1843b, 368.
[477] Ibid., 370.
[478] Nicholson 1845, 229.
[479] Muspratt and Hofmann 1843b, 368-369.
[480] Ibid., 369-370.

consequences for the acceptance of substitution theory and the formulation of the ammonia type but I will show that it also laid the foundations for his elucidation of the constitution of the natural alkaloid coniine.

## Synthesis and the Constitutional Analysis of Coniine

According to standard accounts such as Graebe's, the development of constitutional knowledge about the natural alkaloids was a consequence of two things. The first was the discovery that alkaloids could be separated into nitrogenous and non-nitrogenous portions in a process similar to the saponification of fats, these two portions then being reunited by synthesis to re-form the original alkaloid. Second was the theory of aromatic structure developed by August Kekulé and others from the mid-1860s onwards.[481] Yet despite the implicit suggestion that constitutional analysis necessarily preceded synthesis, Graebe's discussion of Ladenburg's 1886 synthesis made little mention of how coniine's constitution had been established, or by whom.[482] In this section I show that even assigning a formula to this relatively simple natural organic substance remained somewhat beyond the limit of expert chemists' empirical grasp well into the second-half of the nineteenth century. I contend that failed syntheses, several of which preceded the elucidation of coniine's constitution, provided important evidence for Hofmann's amendment of coniine's formula and clues which were crucial in solving the puzzle of its constitution. And I argue that, although constitutional knowledge certainly made it easier for chemists including Hofmann to *conceptualise* synthetic routes to coniine, there remained a huge gulf between understanding how a substance like coniine *might in principle* be made and *actually achieving* its synthesis.[483]

Hemlock (*Conium maculatum L.*) had long been of interest for its poisonous properties when, early in the nineteenth century, apothecaries and chemists began trying to isolate its active principle. The name *Coniin* appears to have been coined by the Geneva apothecary Jean Peschier for an alkaline extract of hemlock, but the isolation of coniine is usually attributed to either August Giseke, then assistant to Johann Schweigger in Halle, or the apothecary Philip Geiger. Giseke was awarded a prize offered by the University of Halle for his isolation of the active principle of

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[481] The saponification of fats involves separating the fatty acid portion from the glycerol portion by alkaline hydrolysis. The sodium salts of fatty acids form the active ingredient of soap.

[482] Graebe 1972 [1920], 365-372. The discussion of coniine is on p. 372.

[483] Müller (1985) contains the only account of this work in the relatively recent historical literature but it contributes little to our understanding of the relationship between constitutional analysis and synthesis.

hemlock, but by the late-nineteenth century the greater chemical purity of Geiger's product attracted increasing recognition.[484] Coniine was first subjected to quantitative organic analysis in Giessen during the early 1840s, as a result of which Vicente Ortigosa proposed the first formula for coniine: $C_{16}H_{16}N$.[485] Another Giessen chemist John Blyth revised Ortigosa's proposed formula in 1849,[486] but the formula $C_{16}H_{15}N$ proposed by Gerhardt in the same year and confirmed by August Planta and Kekulé in 1854 became the generally accepted formula of coniine during the 1850s, 60s and 70s, during which time it was converted to $C_8H_{15}N$ following the adoption of a new atomic weight for carbon. Planta and Kekulé determined in 1854 that coniine was a secondary amine, but otherwise its constitution remained unclear throughout this period.[487]

Far from being deterred by this lack of constitutional knowledge, Hugo Schiff – then Professor of Chemistry at the *Ististuto superiore* in Florence – actively sought constitutional information through the attempted synthesis of coniine.[488] In 1870 Schiff proposed a new constitutional formula for coniine in a short paper published in the *Berichte* of the German Chemical Society entitled: *First Synthesis of a Plant Alkaloid. Synthesis of Coniine.*[489] Schiff's claim was dramatic, but chemists' response was rather muted. An abstract of Schiff's work published in the British *Journal of the Chemical Society* suggests why this was so.[490] Schiff may have "succeeded in producing by synthesis a product which possesses the characteristic properties of the active principle of hemlock", but the abstracter would admit no more than that "there is obtained amongst the other products, a final one which has the composition of the alkaloid in question".[491] In other words, the substance prepared by Schiff was chemically similar to coniine, but he had not provided sufficient evidence to establish the identity of his artificial base with natural coniine. As Schiff himself admitted, he had not obtained his product in sufficient quantity or purity to analyse it, and his identification therefore relied principally on its physiological properties:

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[484] Bley (1863) gave a fulll account of coniine's early history. Stoehr (1886) defended the superiority of Geiger's claim.
[485] Ortigosa 1842.
[486] Blyth 1849b.
[487] Planta and Kekule 1854.
[488] Schiff's biographical information is taken from Wichelhaus 1915, and Betti 1916.
[489] Schiff 1870.
[490] J.B. 1871, referring to Schiff's paper in *Pharm. J. Trans.*, iii, 605.
[491] J.B. was rather generous here, since the composition of Schiff's product had not been established by analysis.

> *This base shows, so far as I have so far been able to convince myself, the reactions and the physical properties of coniine. It acts as a powerful poison and from some experiments, which I have carried out together with my brother [the physiologist Moritz Schiff], it shows poisoning phenomena which are completely characteristic of coniine.*[492]

Publishing this paper in the *Berichte* must have seemed to Schiff an effective way to raise his visibility in Germany, but his failure to present any quantitative analytical data whatsoever critically undermined the validity of his claim.[493] Why, then, did the editors of the *Berichte* agree to publish Schiff's work? For one thing, the *Berichte* was then a relatively new journal in a field where several others were already well established. Its editors were unlikely to refuse to publish what might well be the first synthesis of a plant alkaloid, thereby giving ground to their competitors. Perhaps more importantly, the Berlin Academy's competition for the synthesis of medicinally useful alkaloids also remained open but without any entrants. Schiff's apparent success provided the earliest indication that a prize-winning entry to the competition might soon be forthcoming, which surely pleased Hofmann. The *Berichte* and its editors had little to lose, and potentially a lot to gain, by publishing Schiff's work.

The outcome for Schiff was rather less positive. Having claimed the synthesis of coniine and been met with a sceptical response, he published three further papers concerning the synthesis of coniine during 1871-3.[494] Without ever admitting in so many words that the substance he had prepared in 1870 was *not* coniine, Schiff gradually shifted his position. Whereas his "artificially prepared base possessed the smell of coniine to the highest degree", he was forced to admit in 1871 that it showed a number of differences in reactivity compared with natural coniine. Nevertheless, Schiff was encouraged that this substance poisoned frogs in a way "which my brother regards as characteristic of poisoning with coniine", so that he wondered whether the "small differences" in reactivity would be explained by the impurity of the substance, or by a case of "fine" isomerism.

A year later Schiff published *Further Information about Artificial Coniine* in which he suggested the name "paraconiine" for the artificial base, explaining that whilst most of its physical properties were at least similar to those of natural coniine, the "chief

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[492] Schiff 1870, 947.
[493] Schiff had obtained his Ph.D. with Wöhler in Göttingen in 1857, but by 1870 he was isolated from the dominant German chemical community, which perhaps helps to explain why he was prepared to make such an important claim on the basis of evidence clearly regarded as inadequate by his peers. Once it became clear that he had *not* synthesised coniine, Schiff adopted a different role as Italian correspondent to the German Chemical Society. Schiff (1872a and subsequent reports) kept readers of the *Berichte* up-to-date with chemical research in Italy.
[494] Schiff 1871, 1872b, and 1873.

difference is rather that the artificial alkaloid possesses no [optical] rotational ability".[495] Only in 1873, in the second of two much more detailed papers entitled *On the Synthesis of Coniine* which were published in Liebig's *Annalen*, did Schiff present an exhaustive comparison of the chemical and physical properties of the substance he had made with those of natural coniine. Now, for the first time, Schiff emphasised the differences between the two, including a "clearly defined chemical difference": natural coniine had one replaceable hydrogen (secondary amine), whereas the artificial base had none (tertiary amine).[496]

These four papers show just how much work Schiff had to do before he was convinced that he had *not* made coniine. They also illustrate what kind of evidence was necessary to settle questions of chemical identity during the early 1870s and how rapidly standards for such evidence were changing at that time. Whereas Schiff had originally been happy to claim chemical identity on the basis of physiological properties alone, he subsequently deployed an increasingly sophisticated battery of physical and chemical properties in the attempt to demonstrate that his synthetic product was coniine. Perhaps stung by other chemists' dismissive reactions to his work, Schiff drastically updated his approach to the problem of chemical identity, with the result that his later papers offer a window onto the state of this art in the early 1870s. A chemical difference was ultimately decisive in this particular case, but the more generally striking feature of Schiff's later papers is the growing body of evidence derived from the measurement of physical properties, including expansion coefficient and optical rotation as well as melting and boiling point. But despite the increasing volume of such evidence, it remained extremely difficult – at least for Schiff – to assess its value in relation to other more traditional characteristics such as smell.[497] Physical properties such as melting and boiling point became decisive criteria of chemical identity during the later decades of the nineteenth century (as I examine in detail in Chapter Four) but in the early 1870s it was far from clear that they should, or indeed could, be used in that way.

Disappointing as the outcome must have been for Schiff, his investigations of this artificial alkaloid, its reactivity and physical properties, and his rationalisation of his

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[495] Schiff 1872b, 42-44.
[496] Schiff 1873, 97-98.
[497] Numerous substances isolated by chemists during the 1870s and 80s smelt extremely similar to coniine, but in 1870 it was far from clear that this smell was not characteristic of a single substance, instead being shared by most substances constitutionally related to pyridine. Hofmann (1884, 827) described the characteristic smell of pyridine bases as "a not to be underestimated means of recognition" for this *group* of compounds.

findings in terms of constitutional formulae, nevertheless provided other chemists with valuable information. One chemist who took particular note was Hofmann. In addition to his interest in the unclaimed Academy prize, Hofmann occupied a senior position in the German Chemical Society.[498] He was also well aware that Schiff's research overlapped to a considerable extent with his own. In the mid 1860s, for example, both chemists had been working with diaminotoluene.[499] More recently, Hofmann had disputed the identity of another of Schiff's synthetic products. On that occasion, Hofmann claimed that a "fleeting comparison of the properties of both substances suffices in order to recognise that apart from their composition they had nothing in common".[500] In the case of coniine, it took rather longer for Hofmann's response to Schiff's work to appear in print. When it did, in one of a series of papers concerning the *Effect of Heat on the Ammonia Bases*, it marked a complete break in the investigation of coniine.[501] According to Hofmann, not only had chemists not yet understood the constitution of coniine, they had been working for almost thirty years with the wrong composition.

The reasoning which led Hofmann to amend the formula for coniine by the addition of two atoms of hydrogen is instructive on a number of points. He criticised the basis on which Planta and Kekulé had assigned the formula $C_{16}H_{15}N$ in 1854, but it was much more important to Hofmann that this formula "has also been in the minds of chemists during all attempts at the synthesis of coniine".[502] Schiff's preparation of an ammonia derivative of butylaldehyde had, Hofmann continued, "been taken for a moment for coniine, until it became evident on more thorough investigation that this base is a tertiary amine". And when Hofmann himself had drawn attention to the fact that dicrotonylamine had the same composition as coniine, "this conception had been based on the generally accepted formula of the hemlock base".[503] I contend that the fact that *neither* of these synthetic products had proved to be coniine suggested to Hofmann that the formula for coniine might be incorrect.

Hofmann re-examined the existing analytical data, criticising Planta and Kekulé's formula for coniine because a "higher hydrogen content was already decisively

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[498] Hofmann was founder and first President of the German Chemical Society, and was re-elected as President in 1872 and 1873.
[499] Schiff (1866, 107) explained that both chemists were working with samples of diaminotoluene provided by Collin and Coblenz in St. Denis.
[500] Hofmann 1871c, 250. The substance in question was *triphenylbiuret*.
[501] Hofmann 1881c.
[502] Ibid., 706.
[503] Hofmann 1879c, 992.

displayed", particularly in Blyth's results.[504] He also presented a new series of analyses of carefully dried coniine. According to Hofmann these analyses, almost certainly performed by his assistant Carl Schotten, "speak unambiguously for the formula with 17 atoms of hydrogen".[505] But Hofmann's most compelling evidence for his amended formula depended on the "displacement process" which took place when the fully methylated iodide salt of coniine (*trimethylconylammonium iodide*) was distilled from alkaline solution.[506] Coniine's new formula ($C_8H_{17}N$) also made better sense of its relationship to the hydrocarbon conylene ($C_8H_{14}$) and other related substances previously isolated and studied by Theodor Wertheim, another Giessen-trained chemist who was then Professor of Chemistry at Graz.[507] More than this, Hofmann explained, "in the production of [conylene] from coniine by means of the reaction I have described a further security for the suggested formula of coniine has been given". It was, Hofmann continued, "worth emphasising that when represented this way, coniine appeared as a simple homologue of piperidine".[508]

Hofmann now emphasised the analogy between piperidine and coniine but, in the absence of detailed knowledge of the constitution of piperidine, this did not cast great light on coniine's constitution.[509] In 1879 Hofmann had suggested that piperidine, a secondary amine produced by decomposition of piperine (the alkaloid in black pepper), might be related to pyridine but this idea still remained without a "factual basis".[510] Cahours' earlier work had shown that the alkyl group $C_5H_{10}$ satisfied two of nitrogen's three valencies, reflected in the formula $(C_5H_{10})^{II}HN$, and this prompted Hofmann to investigate the nature of this bivalent group.[511] Hofmann eventually isolated a new hydrocarbon piperylene, to which he assigned the formula $C_5H_8$, but his results remained otherwise inconclusive.[512] Thus although the analogy Hofmann proposed enabled him to represent coniine by the formula $(C_8H_{16})^{II}HN$, he warned that there might still be "fundamental deviations in the

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[504] Hofmann 1881c, 706-707.
[505] Hofmann (1881c, 707-708). Hofmann thanked Schotten on p. 713.
[506] Hofmann 1881c, 705. This reaction is now known as the *Hofmann elimination*. See also Hofmann 1851, 263 and 1881a, 1881b.
[507] Hofmann (1881c, 710-711) referred to Wertheim (1862 and 1864).
[508] Hofmann 1881c, 712.
[509] Keas (1992) discussed the influence of analogical reasoning on the development of Hofmann's research programme.
[510] Hofmann (1879a, 988).
[511] Cahours 1853, 101.
[512] 1881a.

atomic structure of the bivalent groups $C_5H_{10}$ [in piperidine] and $C_8H_{16}$ [in coniine]".[513]

The next task, Hofmann proposed, was to produce piperidine and coniine from the hydrocarbons piperylene and conylene by the addition of ammonia. Achieving this transformation would serve a two-fold purpose. It would demonstrate the reversibility of the processes by which piperylene and conylene had been formed in the first place, but Hofmann also anticipated that this transformation would be used in the eventual syntheses of piperidine and coniine.[514] According to Hofmann, identifying conylene as the hydrocarbon precursor to coniine resulted in "a simpler formulation of the problem [of synthesising coniine]" so that "its solution appears to move a step closer". In this one respect, Hofmann's view of the constitution of alkaloids remained essentially unchanged since the early 1840s, but he was also hopeful that his new method of constitutional investigation by exhaustive methylation could be applied to "other more complicated nitrogen compounds, whose nature is still concealed". Although Hofmann's approach to constitutional investigation depended on new reactions which produced previously unknown products, his goal remained understanding natural alkaloids, and Hofmann described nicotine, pyridine and quinoline as "already drawn into the circle of my research".[515]

Two years later, Hofmann was able to provide direct experimental evidence for the constitutional relationship between piperidine and pyridine when, assisted by his student Franz Mylius, he succeeded in producing pyridine from piperidine.[516] Starting from his earlier study of the action of bromine on coniine, Hofmann now claimed that similar experiments on piperidine produced "a not insignificant quantity of pyridine". He had attempted to reverse this transformation but, although the analogous oxidation and reduction of monobrominated coniine had succeeded, Hofmann was unable to reduce pyridine to piperidine.[517] Hofmann's conversion of piperidine into pyridine was important because it implied that coniine was also constitutionally related to pyridine. This relationship was confirmed beyond doubt

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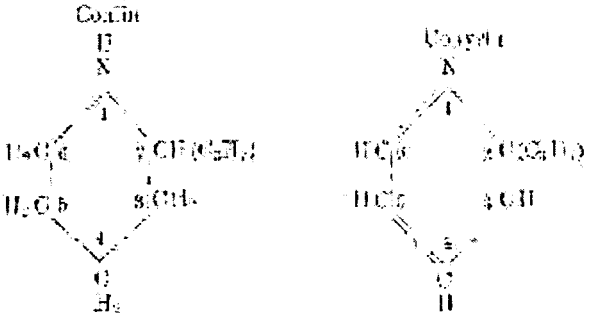
[513] One of Hofmann's key pieces of evidence in support of such a difference was the disparity in their effectiveness as poisons: variance in physiological activity could be useful in suggesting constitutional differences, but it was dangerous to infer constitutional identity from similar physiological behaviour.
[514] See Klein and Lefèvre (2007, 230) on the importance of reversibility in developing analytical understanding of substances.
[515] Hofmann 1881c, 713.
[516] Hofmann 1883a, 587. Hofmann thanked Mylius most warmly for his support on p. 591.
[517] Ibid., 588 ("eine nicht unerhebliche Menge von Pyridin") and 590. Whereas Hofmann (1881b, 667-669) had previously dismissed König's proposal that piperidine was a fully reduced pyridine, he now (1883a, 587) accepted that piperdine could be oxidised to pyridine, although it had been extremely difficult to obtain sufficient pyridine for analysis by this route.

when, in 1884, Hofmann published the conversion of coniine into a new base conyrine by the action of bromine in alkaline solution, and the reverse conversion of conyrine into coniine.[518] Conyrine, Hofmann declared, was "an indubitable pyridine base".[519]

Hofmann's investigation of conyrine resolved an additional aspect of this constitutional puzzle. He found that conyrine could be decomposed to α-pyridinecarboxylic acid, which confirmed that conyrine – and therefore also coniine – contained an alkyl group in the position *ortho* (next) to nitrogen.[520] As a result, Hofmann suggested that coniine and conyrine might be regarded according to the following graphical formulae:[521]



In 1885 Hofmann was able to propose a constitution for coniine in which only the nature of the propyl group (i.e. whether it was straight or branched chain) remained to be ascertained. This remarkable achievement had involved Hofmann, his assistant Schotten and his student Mylius in years of work, including the development of several methods later incorporated into chemists' standard repertoire of constitutional analysis.[522]

Hofmann also recognised that establishing coniine's constitutional relationship to pyridine brought its synthesis "a step nearer", and he continued by outlining two potential synthetic routes to coniine, the first of which was already being investigated by Albert Ladenburg, now Professor of Chemistry in Kiel. Ladenburg's chosen route involved the production of a suitably alkylated pyridine which could be converted into coniine by reduction. Hofmann, however, anticipated that it might prove easier to

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[518] Hofmann 1884, 829.
[519] Ibid., 832. Hofmann (1885a, 128) explained that this discovery provided a "factual basis" for the earlier "outspoken suggestion" of A. Wischengradski and W. Königs that coniine was related to pyridine, which Hofmann had hitherto regarded as unfounded speculation.
[520] Hofmann (1885a, 128 and 1884, 830) argued that the *ortho* position was most likely.
[521] Hofmann 1885a, 129.
[522] Particularly important were the reactions now known as the *Hofmann rearrangement* and the *Hofmann elimination.*

alkylate piperidine directly, and he concluded by thanking his student Paul Ehestädt who was already carrying out experiments "in this direction".[523] These experiments seem not to have made much progress: they were never published and within a year, still well before Ladenburg published the synthesis of coniine in 1886, Ehestädt was involved in Hofmann's study of the coniceïnes, a series of artificial organic amines derived from coniine.[524] Hofmann's constitutional knowledge enabled him to propose potential synthetic routes to coniine based on existing or plausible chemical transformations but, although Hofmann clearly considered these transformations to be conceptually quite straightforward, he and Ehestädt were not successful in synthesising coniine.

How can we explain this failure? It is worth noting that, by 1885 Hofmann's active chemical career was drawing to an end. As he himself acknowledged when confronting the many questions raised by his study of the coniine group: "I cannot know whether I shall be permitted to complete this investigation".[525] In fact, Hofmann published only a small number of scientific papers after 1885, none of which related to coniine or other alkaloids. His two 1885 papers *Towards Knowledge of the Coniine Group*, moreover, reflected the breadth of Hofmann's research interests. Although Hofmann had set Ehestädt to attempt the synthesis of coniine, he soon redirected his student's efforts towards a more systematic study of coniine and its derivatives, and of how these compounds fitted into and extended the existing system of classification of nitrogenous organic bases.[526]

Synthesising coniine proved considerably more difficult than Hofmann had anticipated and so it is worth asking, as Hofmann presumably did, what was at stake in pursuing this goal. For one thing, the synthesis of coniine offered none of the financial and social rewards Hofmann had long anticipated would result from the artificial production of valuable, medicinally useful alkaloids such as quinine. Had his research opened up a potential route to the synthesis of quinine, then Hofmann might well have diverted resources in that direction but as it was he chose to concentrate his efforts elsewhere. Its apparent conceptual triviality probably made the synthesis of coniine appear scientifically rather uninteresting to Hofmann. In addition, although he knew that Ladenburg was hoping to achieve the synthesis of

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[523] Hofmann 1884, 833.
[524] Hofmann (1885a and b) were submitted in January 1885, nine months after Hofmann 1884. Hofmann (1885a, 131) explained that Ehestädt had taken over from Mylius after the latter's departure for Freiburg.
[525] Hofmann 1885a, 131.
[526] Hofmann 1885a and b.

coniine by the alkylation and subsequent reduction of pyridine, Hofmann had already insured himself against Ladenburg's success. His original announcement of Ehestädt's work suggested that Hofmann believed the direct alkylation of piperidine would produce coniine more easily – and quickly – than Ladenburg's alternative route, but it also claimed that Ladenburg's key transformation – the alkylation of pyridine – was nothing more than an *application* of Hofmann's own method for the alkylation of aniline. Whoever synthesized coniine, Hofmann had staked his claim to a fair share of the credit.[527]

Closer to home, Schotten had sought and been granted Hofmann's permission to work on coniine after leaving Hofmann's laboratory in 1881 for a position in the physiological institute in Berlin. I reserve discussion of Ladenburg's work for Chapter Four but devote the remainder of this section to a comparison of Schotten's independent research on coniine with work performed under Hofmann's guidance by his student Mylius during the same period. This comparison reveals the strengths and weaknesses of Hofmann's mature research approach as it was practised and taught in Berlin in the 1870s and 80s, and I use this analysis to argue that neither Hofmann nor any of the chemists he trained were equipped to synthesise coniine.

Schotten and Mylius both trained in Hofmann's Berlin laboratory (where they were awarded the Ph.D. degree in 1878 and 1883 respectively) and where, as I have already described, they both contributed to Hofmann's research on coniine during the early 1880s.[528] A comparison of their work is made particularly instructive because of the discrepancy in ability between the two men. Whereas Schotten was a diligent, competent student whose doctoral dissertation had made "a valuable contribution to the history of aromatic compounds" by applying the reaction recently discovered by Carl Reimer and Ferdinand Tiemann in Hofmann's laboratory, Mylius had prepared an entirely new class of organic compounds, the thiol bases (*mercaptamines*).[529] His dissertation elicited the highest praise from Hofmann, who declared Mylius to be "a man of clear understanding, extensive knowledge, a rare

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[527] Hofmann 1884, 833.
[528] Biographical information on Schotten and Mylius is taken from Poggendorff (1904): 1051 (Mylius), and 1347 (Schotten). See also *Neue Deutsche Biographie*, Vol. XVIII (Berlin: Duncker and Humblot, 1997): 665-666, on Mylius. Schotten assisted Hofmann with his investigations of the action of heat on amines: Hofmann 1881a, b and c. Mylius' work on the action of bromine in alkaline solution on amides and amines is discussed below.
[529] Humboldt-Universität zu Berlin, Universitätsarchiv zu Berlin, Phil. Fak. 250, p. 54 (Hofmann's report on Schotten's dissertation). Schotten's Ph.D. was published in Tiemann and Schotten 1878.

degree of observational ability and unusual experimental talent."[530] So whilst Mylius was more than capable of executing his teacher's most demanding experimental wishes, Schotten's work illustrates what a hard-working but less outstandingly talented young chemist could achieve once removed from the supportive environment of Hofmann's laboratory.

Schotten published five papers between 1882 and 1884 dealing with the oxidation of piperidine and coniine. Hofmann's investigative approach is easily discernable in Schotten's papers, which show more clearly than any of Hofmann's own publications where the challenges of such work lay. In his first paper concerning the oxidation of piperidine, for example, Schotten persisted in subjecting one compound after another to the same chemical transformation, carefully purified, analysed and characterised the products, but was able to draw no conclusion at all from his results. Moving from one piperidine derivative to another was clearly driven by the kind of analogical thinking Schotten had learnt from Hofmann, but there seems to have been no other rationale for the experimental work Schotten performed.[531]

The difficulties Schotten encountered are even more apparent in his attempts to draw constitutional conclusions from the results of his experiments. Following attempts to oxidise coniine derivatives Schotten considered two alternative possibilities: that coniine was "a hydrated and substituted pyridine"; or that it did not contain a ring. In the former case, Schotten believed that the isolated oxidation products could have been formed neither from an ethyl nor a propyl group in coniine. "[I]t follows from this with complete certainty", Schotten concluded in 1882, "that coniine is not a propylhydropyridine [i.e. a propylpiperidine]", not realising until 1884 – following Hofmann's demonstration that coniine *was* in fact a propylpiperidine – that this interpretation was incorrect.[532] It was, he now admitted, "indifferent, which groups of atoms are attached to the [piperidine] ring".[533] Schotten's training had equipped him with investigative skills, including the ability to perform delicate and potentially dangerous manipulations, but without Hofmann's chemical experience he was largely incapable of converting the experimental results he obtained into meaningful knowledge.

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[530] Humboldt-Universität zu Berlin, Universitätsarchiv zu Berlin, Phil. Fak. 260, p. 6 (Hofmann's report on Mylius' dissertation).
[531] Schotten 1882a. Schotten explicitly referred to "the analogous experiment" in the fn. on p. 426.
[532] Schotten 1882b, 1950.
[533] Schotten and Baum 1884, 2549. The intervening papers were: Schotten 1884a and b.

Mylius, meanwhile, assisted Hofmann in his extended study of the effect of bromine in alkaline solution on amides and amines, including the isolation of α- and β-coniceïne (described below).[534] Although superficially similar to Schotten's work in that it investigated the effect of a single set of reaction conditions on a variety of starting materials, this series of publications was driven by far more sophisticated chemical logic. Hofmann sought confirmation that the observed transformation of acetamide reported in the first paper was typical for the amides as a class, also undertaking an investigation of the mechanism of what he had already recognised must be a multi-step process.[535] From the outset, this work depended on the combination of (Mylius') acute observation and meticulous experimental practice with (Hofmann's) ingenious choice of substrate in order to elicit useful information.[536] Where a particular avenue of research seemed unpromising – as for example in the transformation of monochloroacetamide (*acetmonochloramid*) – it was quickly abandoned in favour of a more productive line of enquiry.[537] Hofmann was also much more cautious than Schotten in drawing conclusions from his results. No doubt partly assisted by vastly greater manpower, but also because he clearly identified experimental ambiguities, Hofmann systematically pursued subsidiary investigations to ensure that each new finding was established beyond doubt.[538]

This ability to discern what questions were *raised* as well as answered by the experimental results he obtained was central to Hofmann's approach. As the final paper in this series describing the unusual behaviour of coniine when treated with an alkaline solution of bromine illustrates, such questions frequently led Hofmann into new and fruitful areas of research, so that his research programme as a whole was remarkable for its breadth as well as its thoroughness. Although he was evidently frustrated because this investigation had "extended in an almost objectionable manner", remaining "far from being brought to a conclusion", Hofmann nevertheless thought it worthwhile to present its "scanty outlines".[539] His interest had been caught by the anomalous behaviour of coniine when exposed to the

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[534] Hofmann 1881d, 1882a, b, c, and 1883b. These papers established what is now known as the *Hofmann rearrangement* or *Hofmann degradation*.
[535] Hofmann (1881d, 2726) described the formation of an "ephemeral intermediate product". Hofmann (1882a) presented "an exhaustive study of the various phases of the process".
[536] I infer from Hofmann's repeated and grateful references to Mylius' assistance that Mylius performed most, if not all, this experimental work under Hofmann's direction.
[537] Hofmann 1882a, 410.
[538] Hofmann (1882a, 415) described additional experiments undertaken to distinguish between two possible constitutional formulae, the established constitution then being confirmed by synthesis.
[539] Hofmann 1883b, 558.

standard reaction conditions. Whereas secondary amines usually produced a primary alkylamine by elimination of alkylenebromide, coniine "in which a bivalent atom complex has taken the place of two hydrogen atoms in ammonia" was converted into a mono-brominated derivative ($C_8H_{16}NBr$).[540] Hofmann treated this new compound with acid and base, reporting that "it undergoes many and sometimes quite remarkable rearrangements, that in particular it is easily changed by separation of hydrobromic acid into analogous bases with less hydrogen", and this single observation led Hofmann to investigate three distinct questions.[541]

First, he was curious as to why piperidine, which like coniine produced a mono-brominated derivative $C_5H_{10}NBr$, otherwise responded very differently to the same treatment.[542] Second, he noticed that one of the bases produced by the action of acid on mono-brominated coniine, a tertiary amine $C_5H_{15}N$, showed a striking resemblance to tropidine, which had recently been isolated by Ladenburg. The two tertiary amines showed similar chemical properties and their melting points differed by only a few degrees but Hofmann, again assisted by Mylius, established by means of a series of chemical transformations that they were nevertheless "quite distinct".[543] Finally, he characterised this tertiary amine as α-coniceïne, also isolating an isomeric secondary amine β-coniceïne, which proved to be the major component of the complex mixture produced by the action of base on mono-brominated coniine.[544]

This comparison of Schotten's independent work with Hofmann's interpretation of Mylius' experimental investigations provides considerable support for my proposal that the synthesis of coniine was a task neither Hofmann nor his students were equipped to perform. One of the great strengths of Hofmann's experimental work was his absolute clarity regarding the extent to which particular conclusions were supported by the available evidence, an acceptance of uncertainty which he managed by constant reliance on painstakingly established methods of chemical transformation. It is no coincidence that numerous new chemical reactions, many of which proved to be of enormous significance in both constitutional analysis and synthesis, were produced by research in Hofmann's Berlin laboratory. And it is

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[540] Ibid., 558-9.
[541] Ibid., 559.
[542] Ibid., 560.
[543] Hofmann 1883a, 590-591.
[544] Hofmann 1885b. Later investigation showed that the production of the tertiary base involved the formation of a second nitrogen-containing ring in what has become known as the Hofmann-Löffler-Freytag reaction. This reaction has been reviewed by Wolff (1963) and Stella (1983).

equally unsurprising that young chemists lacking Hofmann's vast chemical resources and experience found it hard to produce meaningful new knowledge using his approach. Working by analogy was relatively straightforward, but dealing with uncertainty and responding to anomalies required both skill derived from long practice and enormous manpower.

For Hofmann and the chemists he trained, moreover, the controlled application of tried-and-tested chemical reactions tended to conceal the practical difficulties inherent in the preparation of a particular synthetic target such as coniine. As a result, they often perceived synthesis in largely conceptual terms – as Hofmann had when, after reporting the conversion of conyrine into coniine, he asserted that: "It only remains necessary henceforth to convert pyridine into orthopropylpyridine (conyrine). One cannot doubt that this will succeed in the same way which has been adopted with success in the alkylation of aniline."

Even though, as Hofmann then reported, Ladenburg had already prepared ethylpyridine by this route, the preparation of conyrine proved considerably more elusive.[545] Hofmann's high-level focus on the constitutional transformation effected by a particular chemical reaction was an extremely powerful aid to taxonomic and strategic thinking, but in this case it caused him to overlook apparently small yet significant differences. Hofmann presented the alkylation of piperidine as merely an *application* of his own, existing method for the alkylation of aniline but, as Ladenburg later complained, this had not been easy to achieve – not least because there was, in fact, no recognised analogy between aniline and pyridine.[546] The perils of thinking at this level of abstraction are also evident in Hofmann's own chosen route to coniine. It was all very well for Hofmann to assert that: "the synthesis of coniine will perhaps be even more simply accomplished through the action of propyliodide on piperidine at high temperature" but, as he and Ehestädt discovered, this was very far from being the case.[547]

I have shown that the relationship between synthesis and constitutional knowledge is a good deal more involved than most histories of chemistry acknowledge. Synthesis could serve as the ultimate confirmation of proposed constitution – and hence of underlying constitutional theory – but it also played an important role in elucidating constitution in the first place. As the case of coniine illustrates, constitutional knowledge was neither a necessary nor a sufficient condition for

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[545] Hofmann 1884, 832.
[546] Ladenburg 1888b, 2.
[547] Hofmann 1884b, 833.

successful synthesis. I have argued that even at the end of his career Hofmann's investigative approach remained deeply imbued with the synthetical approach he had first learnt in Giessen some forty years before and that, although it was highly effective in constitutional analysis, it was not well suited to the target-oriented synthesis of natural products. In the conclusion of my case study of coniine in Chapter Four, I will show how a younger generation of chemists including Ladenburg developed a new chemical practice aimed at exactly that goal.

The present work also prompts a re-evaluation of the relationship between natural and artificial substances as both starting materials and the targets of synthesis. I have argued that Hofmann was originally prompted to study the artificial base aniline and its derivatives by their constitutional simplicity and more manageable physical properties. On the other hand, his experience of working with piperidine and coniine showed that greater constitutional simplicity did not always equate to greater ease of handling. Hofmann made pragmatic decisions, quickly shifting his attention to the more tractable experimental subject, regardless of whether it was natural or artificial. Because they have tended to partition his work on exactly those lines, historians have gained a rather fragmented insight into Hofmann's approach to constitution, reactivity and synthesis. By treating Hofmann's work as a coherent whole, I have illustrated how knowledge of artificial substances contributed to understanding of natural ones and *vice versa*, showing how Hofmann's *synthetical experiments* led him to develop powerful and durable tools of constitutional analysis, and reactions which remained in the repertoire of synthetic organic chemists for more than a century.

## Conclusion

This chapter shows that synthetic organic chemistry lacks a history which explains its origins and development within academic laboratories and acknowledges its changing meaning and purpose. It also explains why writing such a history is not easy. For one thing, chemists' histories – both contemporary and more recent – have usually been written in such a way as to obscure those changes. Only by placing these sources, which historians have assumed embody accuracy and neutrality, in historical context can we regain a historical perspective on the events they describe. One important feature recovered by this approach is the complex relationship between theory and experiment in nineteenth-century organic chemistry. Whereas historians have tended to identify the development of organic chemistry in this period with a succession of isolated theories of constitution and transformation, this account shows that such theories cannot be separated from their accompanying

experimental practices. As historians, we cannot understand questions preoccupying nineteenth-century organic chemists – *Is this substance pure? What is this substance? What is the course of this reaction?* – without reference to contemporary chemical practice. Only a history of practice, moreover, enables us to learn how chemists answered those crucial questions.

The preceding chapters examined the delicate balance between theory and practice in Liebig's laboratory in some detail. I have claimed here that Hofmann's synthetical approach to research relied on the same *philosophy of practice.* In Giessen that philosophy of practice guided analysts as they fitted formulae to the results of quantitative organic analysis, referring to both theories of chemical constitution and their accumulated experimental knowledge of the substance under investigation and its decomposition products. Hofmann and his students applied well-studied chemical reactions to transform relatively simple starting materials into more complicated products and, like Giessen analysts, they arrived at the most likely interpretation of their results by balancing the relative certainty of reaction, analysis and theoretically plausible constitution.

In Liebig's laboratory, the indeterminacy of analytical data was managed using empirical procedures and by reliance on a relatively small number of standard decomposition processes that produced constitutionally simple products. A quarter-of-a-century later, the balance of uncertainty looked rather different. Analytical data were much more secure and – thanks in no small part to Hofmann's own research programme – many more reactions were known and understood. The focus of uncertainty for Hofmann and his students was the constitution of their reaction products, whereas in Giessen it had been the formula of the starting material. In both cases, however, chemists produced reliable new knowledge from often indeterminate results by skilfully weighing-up experimental evidence and theoretical convictions. I therefore contend that Giessen analysis and early synthetic organic chemistry depended on the *same* philosophy of practice, and the *same* kind of network of manipulative and interpretational skills acquired within an intimate laboratory environment.

When considered from this perspective, analysis and synthesis in organic chemistry emerge as complementary elements of a single practice rather than discrete and even opposite practices, countering the juxtaposition frequently derived from Berthelot's programmatically philosophical *Organic Chemistry founded on*

*Synthesis*.[548] This appreciation has important consequences. First, it brings organic chemistry into line with inorganic, a point which has a fundamental impact on the historiography of disciplinary divergence and convergence in nineteenth-century chemistry. The synthesis of organic substances certainly confirmed the unity of chemistry, as Brooke has argued, but *synthetical experiments* followed so hard on the heels of the emergence of organic chemistry as a distinct sub-discipline that it is hard to believe chemistry was really *that* divided in the early decades of the nineteenth century.

Second and closely related to the theory-practice relationship mentioned above, it shows that Hofmann's approach to doing *synthetical experiments* had a lot more in common with analysing organic substances than has previously been recognised. This continuity between analysis and synthesis in organic chemistry helps us to make a lot more sense of the repeated claims of Hofmann, Baeyer and others to be the inheritors of Liebig's legacy. They represented that legacy as principally connected to Liebig's development of laboratory-based training and his introduction of the *Kaliapparat*, ideas which have been fairly uncritically repeated in histories of chemistry ever since. My account of how Hofmann drew upon the research methods developed by Liebig in the field of organic analysis shows that his inheritance was very much richer than that. There is an important continuity of practice between Liebig and later generations of organic chemists, but this did not derive from the fact that organic combustion analysis using the *Kaliapparat* remained an essential component of laboratory training from the 1840s onwards. On the contrary, mistakenly identifying continuity with method and broad pedagogical approach rather than with a higher philosophy of practice has tended to mask important changes in the pedagogy and experimental technique of organic chemistry during the nineteenth century.

Changes of exactly these kinds are visible in the constitutional analysis and eventual synthesis of coniine, these achievements having occupied able organic chemists during the approximately fifty years which spanned the emergence of construction rather than constitutional analysis as the dominant goal of organic synthesis. Even Hofmann's approach, though this continued to have the predominantly analytical goal of increasing understanding of coniine and its relationship to other nitrogenous organic bases, depended on a wide range of experimental methods – for example, the sealed tube reaction – whose establishment as a major technique of synthetic

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[548] Berthelot 1860.

chemistry post-dated the heyday of the Giessen laboratory.[549] Recovering a sense of the problems faced by organic chemists of Hofmann's generation helps us to see the sheer scale of the work involved in moving organic chemistry beyond the *impasse* which so frustrated Liebig around 1840. Whereas the difficulty of assigning chemical identity, for instance, has previously escaped historical attention, it emerges from this history of practice as a central issue in chemists' developing concept of pure substance and an important causal factor in the switch from analysis to synthesis.

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[549] Frankland (1850) described the development of the sealed tube reaction in his work on the hydrocarbon radicals.

# Chapter Four: The Glassware Revolution and the Practice of Synthesis

> *Everyone is familiar with the wonderful properties of glass. Transparent, hard, colourless, unchanged by acids and most other liquids, and, at certain temperatures, more plastic and flexible than wax, it takes, in the hands of the chemist and in the flame of a proper lamp, the form and shape of every piece of apparatus required for his experiments.*
>
> *Justus Liebig (1859)*[550]

## Introduction

I concluded Chapter Three by claiming that the practice of synthetic organic chemistry during the second-half of the nineteenth century involved the development of new experimental techniques, some of which provided the means for executing novel chemical transformations whilst others aimed to resolve the problem of assigning chemical identity. In this chapter I show that many of these techniques made novel uses of glass apparatus, and I argue here that the practice of synthesis as we know it could not have developed without what I call the *glassware revolution*.[551] Of course there is nothing new in the observation that chemists' use of glass apparatus increased dramatically during the nineteenth century, nor in the idea that many chemists learnt glassblowing as part of their training.[552] Until now, however, there has been little attempt to explain or characterise these changes, nor to examine their consequences for chemical practice.[553]

In the first half of this chapter I describe how and why early-nineteenth century chemists laid the foundations for a new kind of chemical practice in glass; in the second I show how this extended *revolution in practice* enabled chemists to overcome important barriers to the development of synthetic chemistry, including the purification and identification of substances as well as the reliable performance of specific chemical transformations. This was partly because, as Liebig explained (see epigraph), working in glass offered chemists unprecedented experimental flexibility, making it possible for them to develop new apparatus in response to

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[550] Liebig 1859, 124.
[551] I have chosen the term *glassware revolution* as a convenient appellation for what I argue here were important changes in the practice of chemistry during the mid-nineteenth century and with only the most general associations to any philosophical notion of the nature of scientific (or other) revolutions.
[552] See, for example, Gay (2008, 56) on glass and glassblowing at the RCC in the 1850s.
[553] Because glassblowing has been regarded as a solely manipulative craft skill requiring little or no intellectual input, very little has been written about glassblowing or the development of chemical glassware. Holmes and Levere 2002 contains some interesting though isolated exceptions, particularly the essays by Russell and Rocke.

specific experimental difficulties, but I show that the large-scale production of standard items of glassware was equally important. In particular, I examine the crucial role played by the specialist chemical glassblower Heinrich Geissler in producing new shared standards by means of which melting and boiling points were transformed into key criteria of chemical identity.

I begin by tracing chemists' appropriation of glassblowing skill, using the work of two of the most outstanding chemical experimenters of the early-nineteenth century Michael Faraday and Jöns Jacob Berzelius to show how chemists began to use glass both in order to become independent of specialist instrument makers and as a means of reducing the cost of their apparatus.[554] Picking up on themes introduced in Chapter One, I contend that these factors were significant in enabling more people in a wider variety of locations to perform experimental chemistry, and that glass and glassblowing therefore played an important role in both the professionalisation of chemistry and its spread beyond major metropolitan centres.[555]

Historians of chemistry have previously expressed a view concerning the implications of chemical glassware for the historiography of nineteenth-century chemistry in only one case, claiming that the development of the *Kaliapparat* was important in the development of large-scale laboratory training in chemistry. As I mentioned in Chapter Two, such accounts have provided very little in the way of a historical context for either the creation of the *Kaliapparat* or its importance. I now return to examine that question in detail, continuing the re-construal of the *Kaliapparat* begun in the opening chapters of this dissertation. I place the development of the *Kaliapparat* in the context of the *glassware revolution* initiated by chemists' production of small-scale glassware by glassblowing and I argue that, whilst the *Kaliapparat* was certainly novel in form, it was a product rather than a cause of this approach to chemical experimentation.

I have argued elsewhere that glassblowing skill was important in the early spread of the *Kaliapparat* across Europe.[556] In this study I examine the first written

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[554] David Gooding (1985) has analysed the uniquely *experimental* nature of Faraday's expertise. Other aspects of Faraday's life and work are examined in Gooding and James 1985.

[555] Inkster and Morrell (1983) is the classic study of metropolitan versus provincial science in Britain. Homburg (1999, 4-5) suggested that the "portable laboratory" contributed to the growth and professionalization of chemistry during the early nineteenth century through the development of a distinct laboratory practice, but did not specify the role played by glassware in that practice. See also Homburg 1998.

[556] Jackson 2006.

instructions for the production of the *Kaliapparat*, published within one of the earliest German texts to present the basics of chemical glassblowing in 1833.[557] I suggest that the *Kaliapparat*, especially because of its pedagogical success, played an important role in mediating the spread of glassblowing skills through the chemical community and that it was therefore significant in extending the geographical spread of the *glassware revolution*. Every student of chemistry in Germany after 1840 – and many elsewhere - learnt to use the *Kaliapparat*, with the result that the construction and management of similar small-scale experimental spaces within glass became a central component of chemists' practical skill. Finally I show how, despite numerous modifications created by chemists and glassblowers to suit a wide variety of experimental situations, both the original *Kaliapparat* and its offspring became functionally defined components in a new chemistry set made of glass. During its long a varied life, therefore, the *Kaliapparat* neatly exemplified the simultaneous vitreous virtues of adaptability and standardisation, and I argue that it was significant in establishing a glassware based chemical laboratory practice which flourished throughout the remainder of the nineteenth and much of the twentieth century.

In the second-half of this chapter I show that both the methods of constructive synthesis and the solution to the problem of chemical identity depended on chemists' combined exploitation of standardisation and adaptability in their ability to design and work with glass. First I return to the problem of chemical identity. I argued in Chapter Three that Hofmann developed his synthetical approach to organic chemistry at least partly in response to this problem, and I showed that this issue remained problematic until well into the second-half of the nineteenth century. In the first part of my case-study of the hemlock alkaloid coniine, for example, I used Schiff's work to illustrate that, despite an accumulation of physical, chemical and physiological evidence, it was extremely difficult for chemists to be sure whether two substances really were identical or not. In the penultimate section of this chapter I show that by 1886, when Ladenburg published the synthesis of coniine, melting and boiling points were becoming decisive, standard indicators of chemical purity and useful identifying characteristics and I explain why and how chemists, assisted by expert glassblowers like Geissler, had repositioned these physical properties from the periphery to the very centre of their practice.

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[557] These instructions (Lafond 1833) substantially predate those included in Liebig's (1837) textbook of analysis.

The first part of my case study of coniine also showed that its constitutional analysis was a protracted business requiring the skills of one of the masters of that art Hofmann, and that the synthesis of coniine was not a straightforward consequence of the determination of its constitution. Attempts to synthesise coniine certainly played a crucial role in resolving questions about its constitution, but the transformational knowledge so produced was not sufficient to enable successful synthesis. I also suggested that Ladenburg was specifically motivated by the goal of producing coniine by synthesis and that this much narrower focus was significant in his success. In the final section of this chapter, which concludes my case study of coniine, I illustrate the specific and limited role of constitutional knowledge in Ladenburg's synthesis of coniine. As much as his constitutional understanding of coniine, I claim that Ladenburg's success depended on a distinct glassware-based manipulative expertise which I argue was essential to the practice of organic synthesis as a constructive art.

Ladenburg's synthesis of coniine shows that purification and characterisation were every bit as important in that practice as any new chemical reaction, and that glass was necessary to all three. By the 1880s chemists had a much clearer notion of what defined a substance as pure and of what evidence could establish chemical identity, but it was still no easy matter either to achieve such purity or obtain that proof. Chemists like Ladenburg blew novel glassware solutions to the practical difficulties of separation and identification as well as transformation, and they collaborated with specialist glassblowers to transform successful innovations into manufactured commodities available throughout Germany and beyond. I contend that the development and rapidly increasing scale of training and research in organic synthesis would have been impossible without this glass chemistry set, and I identify the emergence of synthetic organic chemistry as an independent sub-discipline with its incorporation into chemical practice. By proposing a new history of glassware in nineteenth-century chemistry, this study of the *glassware revolution* therefore prompts a revised view of the practice of organic synthesis and, more generally, of the historiography of nineteenth-century chemistry.

## The Glassware Revolution

> *Frequent occasion has occurred in the preceding parts of this volume for the description of apparatus formed partly or altogether of glass tube. The object of this section is to shew the important uses of apparatus of that description. The facility with which it supplies the absence of many complicated instruments; the consequent economy and readiness of chemical practice; and the peculiar advantages of it when rare and valuable substances are under examination, are the inducements to collect the information upon this subject into one focus.*
>
> *Michael Faraday (1827)*[558]

Numerous early-nineteenth century chemists feared that the difficulty of obtaining adequate equipment presented a serious obstacle to the pursuit of practical chemistry, and hence to the development of their discipline.[559] Faraday's *Chemical Manipulation*, first published in London in 1827, addressed concerns of exactly this nature and in doing so it explains both why chemists perceived this restriction to be a particular problem and how they anticipated that it would be overcome. For one thing, Faraday and other chemists of the day believed chemistry to be the most experimental of sciences in which – unlike astronomy, botany or zoology – mere observation revealed little.[560] As a result, chemistry depended on what Faraday called the "*art of experimenting*" which was facilitated by "habits of correct and delicate manipulation".[561]

Without the ability to perform experiments successfully, Faraday argued, it was impossible for the student of chemistry either to confirm existing results or to develop new knowledge. In Faraday's opinion, moreover, "the numerous and useful works on Chemistry now extant" did not cater for this student audience, which *Chemical Manipulation* was explicitly designed to serve. Rather than discussing "the *principles* of the science", Faraday presented a detailed description of experimental methods, followed by a series of recommended practical exercises using apparatus which was, as the epigraph says, often "formed partly or altogether of glass tube".[562] In this section, I describe Faraday's approach to the use of glassware in chemical experimentation, and how he sought to teach such skills through the medium of a book. I argue that *Chemical Manipulation* was strongly influenced by Berzelius' earlier innovations in chemical practice, and I show how it became a model for numerous other texts on practical chemistry in general and

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[558] Faraday 1827, 391.
[559] See, for example, Longchamp (1823) on the importance of accurate balances in quantitative analysis.
[560] Faraday 1827, i-ii.
[561] Ibid., vi-vii.
[562] Ibid., vii, italics in original.

chemical glassblowing in particular. Taken together, these books demonstrate chemists' increasing reliance on glass and glassblowing to supply a growing diversity of equipment over a dispersed area at relatively low cost.

*Chemical Manipulation* incorporated an egalitarian ideal according to which the practice of chemistry should be disseminated as wide as possible, both socially and geographically. By educating his readers in the "general principles upon which apparatus is formed", Faraday hoped to develop "that *contrivance*, by which the wants of the operator may be obviated; and therefore *small, temporary*, and *generally useful* apparatus, will be pointed out as often as possible".[563] It was important to Faraday that skilful manipulation "diminishes the expense both in materials and apparatus", and the use of glass – which Faraday termed "Tube Chemistry" – was an essential component of this ability.[564]

Faraday described the uses of a huge range of glass apparatus formed from glass tubes by "the methods of softening, bending, and blowing of glass by means of a lamp and blow-pipe".[565] Working glass tubes, either with a table blowpipe or "by means of the common spirit-lamp and mouth blow-pipe" was, Faraday claimed, "daily useful". Presumably in the attempt to encourage would-be chemists in the provinces, Faraday emphasised that:

> *The attainment of a ready practice on these points, together with that of a facility in effectually substituting an apparatus or vessel at hand, for another that is wanting, are, perhaps of all other experimental acquirements, those which render the chemist most independent of large towns and of instrument-makers.*[566]

Faraday's model "independent" chemist might well have been the Swedish chemist Berzelius, who had introduced the simple "test-glass" or test tube to chemistry over ten years earlier as a more economical alternative to earlier footed varieties.[567] Although he travelled to London in 1812 – where he visited the Royal Institution in order to hear Davy's lectures – and to Paris in 1818-1819, Berzelius' career was spent mainly in Stockholm, far away from the hub of European scientific life.

According to his Swedish biographer Erik Jorpes, Berzelius declared himself much impressed by the "amount of work in chemistry that is done in Paris". This was

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[563] Ibid., viii, italics in original.
[564] Ibid., vii (quotation); and 391 ("Tube chemistry").
[565] Ibid., 391-424, and 482.
[566] Ibid., 482-483.
[567] The new form of test glass was not just cheaper; it also allowed the analyst to heat the tube's contents, which was important for many new processes in qualitative analysis. Berzelius (1814b, 403-4) described the development of combustion tubes from simple glass tubes of "diameter between a half and five-eighths of an inch", closed at one end.

partly due to the large number of laboratories devoted to research, but Berzelius also reported that "there are several dealers specializing in chemical glassware whose stock is a source of astonishment to a poor Stockholmer who, when he needs a simple retort, cannot obtain it in less than three months".[568] Perhaps because of this isolation Berzelius applied his skill with the blowpipe, acquired through mineralogical analysis, to glassblowing, becoming a consummate innovator of chemical apparatus.[569] I described in Chapter One, for example, how in 1814 Berzelius rejected the combustion apparatus of Gay-Lussac and Thenard in favour of his own combination of inexpensive glassware made largely from glass tubes.[570] Even though his method as a whole was considered rather time-consuming and difficult, many elements of Berzelius' apparatus were widely adopted and it certainly represented one solution to the problem of how to do quantitative organic analysis without the resources and facilities available to *élite* Parisian chemists.

The similarity in their approach, and between some of the simpler items of glassware they described, suggests that Faraday drew on Berzelius' work when developing his *Tube Chemistry*. The two men certainly knew and admired each other's work. Berzelius called Faraday's isolation and analysis of benzene "the most important chemical discovery" of 1825.[571] In 1831, Faraday wrote to the Secretary to the Royal Society John George Children, himself the translator of Berzelius' mineralogical text *The Use of the Blowpipe*, recommending Berzelius for the Copley Medal.[572] Faraday's nomination was based mainly on the French edition of Berzelius' *Treatise on Chemistry*, the first four volumes of which had been published between 1829 and 1831.[573] In Faraday's opinion, this work alone was "a full and sufficient reason for adjudging the medal to the author [Berzelius]". Having listed Berzelius' most important publications in the *Annales de Chimie* since 1827, Faraday concluded: "I have not thought it necessary to insist upon Berzelius' deserts.

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[568] Jorpes 1966, 82.
[569] Berzelius (1821, 7) described learning mineralogical analysis using the blowpipe from Johann Gottlieb Gahn, but I have been unable to discover how he acquired his skill in glassblowing.
[570] Berzelius 1814b.
[571] Berzelius (1827, 92-104) gave a detailed description of Faraday's isolation and analysis of *bicarburet of hydrogen*, now called benzene.
[572] The Swedish edition was published in 1820, followed in 1821 by the German translation cited above. I have also examined the English edition (1822), dedicated by its translator Children to Sir Humphry Davy, then Honorary Professor of Chemistry at the Royal Institution.
[573] Berzelius 1829-1833.

No one who knows any thing of chemistry can doubt but that he merits it most highly".[574]

Although published several years after *Chemical Manipulation*, the fourth volume of Berzelius' textbook provides a useful means of comparing the views of Berzelius and Faraday on the role of glassware in chemical practice. This volume, published in Wöhler's German translation in 1831 and in French two years later, was subtitled *Chemical Operations and Apparatus*.[575] Even before it was published, the Professor of Chemistry in Berlin Heinrich Rose, who had studied with Berzelius, heralded *Chemical Operations* as making the description of chemical apparatus largely unnecessary in his own *Manual of Analytical Chemistry*:

> *The description of the practical contrivances employed in Analytical Chemistry, is almost entirely passed over. For the introduction of most of these contrivances, and for the greatest improvements they have received, we are indebted to Berzelius. He has accurately described them in the Fourth Part of his System of Chemistry, with the translation of which (*into German*) Professor Wöhler is now occupied. It appeared to me, therefore, to be unnecessary to describe them in this Manual.*[576]

Berzelius intended *Chemical Operations*, which contained "the fruits of experience" to assist "the beginner who lacks the teacher's presence" but, although it included an extended section on the use of the blowpipe for glassblowing, Berzelius was adamant that glassblowing could not be learnt from a book.[577] Whereas Faraday intended *Chemical Manipulations* to guide the student through a course of private study including simple glassblowing, Berzelius saw his book as a useful aid to, but certainly no substitute for, personal experience and face-to-face instruction. *Chemical Operations* included "some words about the relevant general actions", but provided "no more detailed instructions" for how to perform certain steps "because such things cannot be learned from a book, but only through practice, after one has previously observed a practiced [glass]blower at this kind of work".[578]

What made Faraday believe it would be possible for students to follow his book without the support of face-to-face instruction? His confidence may partly have resulted from his own success as a solitary learner combined with limited teaching experience, but there is also an important difference between the kinds of glassware

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[574] Faraday to Children, 21 November 1831, Letter 521 in James 1991, 588. The only Copley Medal for 1831 was awarded to the astronomer George Airy, though Faraday's recommendation may have contributed to Berzelius' receipt of a Copley Medal in 1836.
[575] I have examined the German edition (1831), published as Vol. IV, part 2 of Berzelius' *Lehrbuch*.
[576] Rose 1831, xi. Emphasis in the original, indicating Griffin's clarificatory insertion.
[577] Berzelius 1825, xii.
[578] Berzelius 1831, 873; 878.

used by Faraday for his *Tube Chemistry* and the more diverse apparatus discussed by Berzelius. The quotation above, for example, was written by Berzelius in relation to the blowing of extremely thin glass bulbs which could then be formed into funnels, a far more complex glassblowing procedure than any described by Faraday. I suggest that Faraday resolved the dilemma of how a would-be chemist could learn by private study at limited cost by restricting his use of glassware to the simplest items, whose construction might reasonably be learnt without instruction from a glassblower. This approach, however, had the disadvantage that it excluded students from forms of chemical experimentation then becoming common in the wider chemical community, which increasingly made use of more complicated glass apparatus produced by the kinds of operations referred to by Berzelius.

It is interesting to ask to what extent Faraday was successful in reaching his intended audience, and how his readers fared when they attempted to follow his recommendations. Answering such questions is, sadly, beyond the scope of the current study but there is one respect in which Faraday's book was extremely successful. Although *Chemical Manipulations* appeared in only three further editions during the following fifteen years, its influence is discernible in books concerned with practical chemistry and with glassblowing, both genres undergoing a rapid rise in popularity in the early 1830s.[579] The first category included popular books written by the instrument makers Fredrick Accum and John Joseph Griffin, both of which ran through numerous editions during the early decades of the nineteenth century. Accum's *Chemical Amusement* and Griffin's *Chemical Recreations* both described "instructive experiments" using relatively simple apparatus, but there was no suggestion in their earlier editions that their readers should manufacture the necessary equipment for themselves. Griffin may have reported William Henry's proposed use of wine glasses as improvised test-glasses but Accum was mainly interested in promoting his own wares, which included "Chemical Chests for amusing experiments" and "Portable Chemical Laboratories, including all the preparations and apparatus necessary for chemical research".[580] By 1838, however, the eighth edition of Griffin's greatly expanded *Chemical Recreations* was subtitled *Chemical Manipulation* and it included an extensive

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[579] Subsequent editions were published in 1829, 1830 and 1842.
[580] Accum 1817. On the introduction and importance of portable laboratories see Gee 1989. Griffin (1825, 73) suggested using wine glasses following William Henry's *Elements of experimental chemistry*, which was first published in 1799. See, for example, Henry 1826, 591-592 (on the detection of arsenic); 624 (on the analysis of limestone). For more on the relationship between Griffin, Accum and Henry, see Gee and Brock 1991, 34.

description of the techniques of glassblowing, mainly reproduced from a small manual published by the French instrument maker Ferdinand Danger in 1829.[581]

This book *The Art of Glassblowing* is the earliest example of a specialist glassblowing manual aimed specifically at chemists.[582] One of Danger's motives was to advertise his re-designed blowpipe – which was recommended by "the cheapness of its price, as well as the simplicity of its use" – but, like Faraday and Berzelius before him, Danger also promoted glassblowing as the means by which chemists could obtain the instruments they needed for a reasonable price.[583] According to Griffin, few copies of Danger's original book were printed but there appears to have been considerable interest in its contents: within just four years it was translated into both English (1831) and German (1833).

The 1831 English "free translation" by Griffin with the publisher John Bumpus hoped by its reference to "toys for recreative philosophy" to include an audience of leisured amateurs who did chemical experiments for fun.[584] The *Preface*, however, indicated that the book also sought a more serious, scientific readership:

> *It is therefore advisable that he who desires to occupy himself in the pursuit of experimental science, should know how to prepare such instruments himself; that, in short, he should become his own glass-blower. 'The attainment of a ready practice in the blowing and bending of glass', says Mr. Faraday, 'is one of those experimental acquirements which render the chemist most independent of large towns and of instrument makers'.*[585]

When Danger's book appeared in Germany in 1833, by contrast, it retained its original title and more serious scientific tone, being aimed at "[y]oung people, especially those who wish to perfect themselves in chemical manipulation". In another tantalising echo of Faraday's *Chemical Manipulation*, Danger's introduction continued to explain that without the ability to shape glass tubes, these young

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[581] Griffin 1838, 238. Griffin (1838, 308) also advertised a "Glass Blower's Lamp ... after Danger's pattern". Gee and Brock (1991, 39) suggested that Griffin travelled to Paris in 1829 in order "to meet (and possibly obtain instruction from)" Danger.
[582] Danger 1829. According to Gee and Brock (1991, 39) Danger was "a glass instrument-maker whose own workshop was a focal point for students of the École Polytechnique". *The Corning Museum Library of Rare Books: 18th and 19th Century* (1989) confirms that Danger's book is the first of its kind. As I discuss in Chapter Five, the vast majority of such books date from the latter decades of the nineteenth century and many of these are much more concerned with the construction of the high-vacuum glassware then in widespread use in physics.
[583] Danger 1833, 2.
[584] Danger 1831.
[585] Ibid., iii.

chemists were "inhibited in their studies, because they were not able to practise the *art of manipulation*".[586]

Friedrich Körner's *Introduction to Glass-working before the Lamp*, which had been published in Germany two years earlier, confirmed the need both for the acquisition of glassblowing skill by chemists and for an effective pedagogical text:

> *It seemed to me not only useful but even, because of the manner in which chemical experiments are now made, necessary to attempt something on this subject [the construction and use of instruments made by glassblowing], because there is nothing available according to my knowledge which deals with it reasonably appropriately.*[587]

This book is especially interesting because Körner, unlike Faraday and – to my knowledge – Danger, had some experience of teaching glassblowing to young science students at the University of Jena. The format of Körner's courses, which had been held every term for some years before 1831, seems to have been the lecture-demonstration, Körner showing his audience "the knack of working apparatus which may be made by means of the lamp" and explaining the "theory of instruments". In Körner's opinion, which he claimed was shared by the faculty at Jena, glassblowing was "not only of great utility in itself" but also helped young people to develop their dexterity, as a result of which "they learnt to handle objects skilfully during many practical scientific manipulations". Körner intended his book to aid his own students by reminding them of what they had heard during "orally given lessons", but he also hoped that it would be "a faithful advisor in difficult cases" to others.[588] It seems that, although he believed personal instruction to be desirable, Körner – like Faraday and Danger – expected that students would be able to learn something from his book. No link with Faraday's *Chemical Manipulation* is suggested by Körner's book, but he certainly based his work to some extent on Danger's, claiming to have improved upon the French text's "innumerable gaps and superficialities".[589]

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[586] Danger 1833, 1. Italics added. I have been unable to ascertain any information about who translated Danger's book into German, or about the circumstances surrounding its publication in Germany.

[587] Körner 1831, vii.

Körner's previous (1824) book dealt with the construction of barometers and thermometers. Other books on glassblowing were published in German during the 1820s and 30s, including the much less comprehensive Rockstroh 1833.

[588] Ibid., 2-4. Körner also referred in somewhat negative terms to Karl Diesing's 1824 *Die Glasschmelzkunst bei der Lampe von einem praktischen Glaskünstler* (not examined).

[589] Körner 1831, 3-4. The first 4 (of 6) plates in Körner's book are identical to those in Danger 1833, the last 2 containing additional information for the manufacture of thermometers and barometers. There is some overlap in the content of the two books – for example, Körner describes Danger's blowpipe and bellows – but Körner's book provides

The appearance of Danger's book in the three major scientific languages of Europe indicates that around 1830 chemists were becoming increasingly dependent on the new kind of glassware recommended by Berzelius. Usually smaller, though frequently more complex, than the flasks and retorts used in chemical and alchemical laboratories for centuries, the new apparatus could be constructed by the chemist himself, once he had acquired the necessary skill in glassblowing. It was widely recognised that this skill could only be developed through practice, preferably assisted by face-to-face contact with a skilled glassblower, but the publication of Danger's book suggests that this was frequently difficult to achieve.[590] As Danger's English translator Griffin explained, workmen were busy in large towns and glassblowers were rare in small ones. Even where they could be found, they were usually "too jealous of their supposed *secrets* to be willing to communicate their methods of operating to strangers, even when paid to do so".[591] It might well be, as Berzelius claimed, impossible to provide written instructions for key aspects of the glassblower's art, but the increasing geographical spread of chemistry meant that for many, learning from a book – however problematic – was the only option.[592] Danger's was the first manual of glassblowing which aimed to provide chemists with the range of skills needed to construct the increasing diversity of chemical glassware, and its rapid transfer across Europe during the 1830s suggests that it was perceived by chemists to be a useful response to a widely felt want. The *glassware revolution* had begun.

## Re-inventing the *Kaliapparat*

> *For anyone who is occupied with chemical investigations, it is an unavoidable requirement to be able to work glass before the lamp, to bend glass tubes into various shapes, to blow bulbs from them, etc.*
>
> *Jöns Jacob Berzelius (1831)*[593]

The preceding section argued that glass apparatus and glassblowing became crucial aspects of the material culture and practice of chemistry during the early-nineteenth century. Chemists' appropriation of glassblowing skills opened up a new world of possibilities, supporting innovation and enabling chemistry's disciplinary

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much more comprehensive coverage of both basic glassblowing operations and the manufacture of barometers, thermometers, etc.

[590] Danger 1831, iii. Both Faraday (1827, 483) and Berzelius (1831, 871) emphasised the absolute importance of practice.

[591] Danger 1831, iii-iv. Direct quotation from p. iv, italics in original. Körner (1831, 2) also noted the rarity of glassblowers experienced in the construction of scientific apparatus.

[592] Berzelius (1831, 873) explained that the "correct nursing of the fire" was the greatest art of glassblowing, for which no instructions could be given.

[593] Berzelius 1831, 871.

growth. Both chemical research and the large-scale laboratory training of chemists developed in ways that would have been impossible in a world without glass. This new vision of the importance of glass to nineteenth-century chemical practice provides an essential and hitherto absent context for Liebig's development of the *Kaliapparat*. As I discussed in Chapter Two, there is rather little direct historical evidence concerning the process by which Liebig produced the first *Kaliapparat*. By reading Liebig's 1830 notebook alongside his correspondence I also showed how difficult it was to make the *Kaliapparat* work, and that this probably involved modifications to its original design, but this still does not explain why Liebig chose to tackle the problems of organic analysis this way. There is, however, a convincing body of circumstantial evidence which, when evaluated in the context of the novel uses of glassware described above, suggests a plausible historical explanation for Liebig's development of the *Kaliapparat*. None of the elements of this explanation is new in itself but, taken together, they suggest more strongly than ever that we should see the *Kaliapparat* as an early and highly influential example of a much more general trend in chemical practice, as a product rather than a cause of the *glassware revolution*.

Existing histories generally consider the technique of quantitative organic analysis to be the most important skill Liebig learnt in Paris, but several pieces of evidence – including the epigraph to this section – suggest that we should accord a similar importance to glassblowing. The experimental work Liebig carried out in Gay-Lussac's laboratory consisted mainly of the analysis of silver fulminate and led to Liebig's first publication, which included a detailed description and several figures illustrating the apparatus he had used (see Figure 5, p. 70).[594] This apparatus combined a modified version of Berzelius' horizontal combustion tube with a graduated glass tube inverted over mercury in which the gaseous combustion products were trapped. The analytical practice of Parisian chemists in the mid-1820s therefore combined the influential French experimental tradition of precision measurement of gases with Berzelian chemical glassware, and the question of how Liebig was able to transfer the experimental practice he learnt in Paris to Giessen acquires an additional dimension as a result.

I have already discussed a number of the difficulties associated with Liebig's move from Paris to Giessen, but I concentrate here on the particular problems caused by the extent to which Parisian analytical apparatus – including the combustion tube –

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[594] Liebig and Gay-Lussac 1824.

was constructed from glass components. If we examine the apparatus (Figure 5) it is clear that, even when reduced to its component parts and carefully packed, such equipment was unlikely to survive a long journey or what Körner called "the unmerciful treatment of the postal workers" undamaged.[595] In the unlikely event that it did so, regular use – especially by students – was accompanied by a permanent risk of breakage.[596] Unless Liebig was unreasonably lucky, this apparatus must have needed repair during the approximately five years it was in use in his Giessen laboratory, and the majority of those repairs are likely to have involved glassblowing.

We know that glassblowing was important to Liebig because he devoted a considerable portion of his visit to Paris towards the end of 1828 to the acquisition of this skill, writing to his wife: "Think, I have taken instruction in glassblowing and made enough progress to be able to make all glass apparatus for myself".[597] It is impossible to say whether Liebig's main objective was to be able to maintain his existing apparatus or whether he was already considering producing new glass apparatus to his own specification – though the latter might legitimately be viewed as an additional outcome of his Parisian experience, since we know that Gay-Lussac was "occupied with ... the design of a factory for *instruments de précision* (thermometers, alcoholometers, etc.)" early in 1824 and continued to publish articles concerned with instrumental innovations until at least the 1830s.[598]

Liebig made several visits to Paris in the years around 1830 and, although I have found no evidence to suggest that he spent more time learning glassblowing, glass remained important to him throughout this period. Glass and glassblowing, for example, were a recurring theme in Liebig's developing collaboration with Wöhler. Wöhler visited Giessen for the first time during November 1831, where he spent most of his time learning Liebig's new method for organic analysis, "a side of chemistry in which I was quite foreign until now".[599] We do not know whether Wöhler took a *Kaliapparat* with him when he returned to Cassel at the end of November, nor exactly when and how he learnt to make Liebig's new apparatus for himself, but it is extremely probable that Wöhler, who had studied with Berzelius in

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[595] Körner 1831, 2-3.
[596] Schaffer (1992, 33) reported Arthur Schuster's observation that "the instruments [in the Cavendish Laboratory] suffered more than the students by their being so freely allowed to come unchaperoned into mutual contact".
[597] Letter from Liebig to his wife, 2 November 1828, in Dechend 1953, 24.
[598] Mitscherlich to Berzelius, 16 January 1824, in Söderbaum 1932, 35-42 (p. 35). According to Crosland (1978, 192-193) [and Child (1940, 98)] Gay-Lussac's partner in this venture was the instrument maker Charles Félix Collardeau du Heaume (1796-1869). Gay-Lussac (1833) included the construction of a low temperature air thermometer.
[599] Wöhler to Berzelius, 24 November 1831, in Wallach 1901, 380-381.

Stockholm, was already a skilled glassblower and so able to acquire that knowledge relatively quickly under Liebig's personal guidance.[600]

Certainly, the correspondence between Liebig and Wöhler shows that glass played an important role in the transfer of organic analysis to Wöhler's new laboratory in Cassel. In January 1832, for example, Wöhler wrote to Liebig: "I am sending all of the suitable glass tubes I could get here. Few enough, therefore I am also enclosing the ones obtained from you".[601] Having returned from Giessen with glass tubes, probably for use as combustion tubes if not for the production of new *Kaliapparate*, Wöhler had sought his own, local supply. Finding the right kind of glass seems not to have been easy even within Germany – Wöhler complained in the same letter that a recent consignment of glassware from Frankfurt was "large, old-fashioned stuff".[602] The high value of "usable" glass tubes is, moreover, clearly indicated by the fact that Wöhler returned to Liebig the tubes he no longer needed.

During 1832 Wöhler received two further items of apparatus from Giessen: a glassblowing lamp and an air pump in Gay-Lussac's design for use in organic analysis.[603] He kept the "very nice and superior" glassblowing table, but sent the air pump on to Gustav Magnus.[604] The original source of these objects is unclear, but it seems reasonable to suppose that they were of French manufacture. In the same letter, Liebig reported that he had ordered three thermometers from the Parisian instrument maker Charles Collardeau. Like the air pump, these thermometers "in which each degree is divided into 5 parts" were "indispensable for organic analyses", and I infer from this that Liebig's analytical practice continued to be based in part on the use of French apparatus.[605] Having learnt glassblowing in Paris using a French glassblowing table, moreover, Liebig is likely now to have supplied Wöhler with something similar. Whatever its origin, Wöhler was clearly impressed by the glassblowing table he received from Giessen and it seems, since he kept "his old Swedish lamp" for his private laboratory, that he probably intended to use it in his new chemical institute in Cassel.[606] Liebig's gifts were intended to equip Wöhler to practise and teach organic analysis in Cassel and they suggest that the early spread

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[600] Wöhler's next letter to Berzelius, dated 1 December 1831, was sent from Cassel. See Wallach 1901, 384-387.
[601] L-W, Letter 74, Wöhler to Liebig, [29] January 1832.
[602] L-W, Letter 74, Wöhler to Liebig, [29] January 1832.
[603] Wöhler to Berzelius, 2 May 1832, in Wallach (1901): 431.
[604] Glassblowing lamp and bellows were usually mounted on a glassblowing table and therefore often considered a single item. The use of an air pump to evacuate the combustion apparatus was essential to the production of accurate analytical results.
[605] L-W, Letter 84, Liebig to Wöhler, 1 May 1832.
[606] Wöhler to Berzelius, 2 May 1832, in Wallach 1901, 431.

of Liebig's system of laboratory training depended on the physical movement of apparatus including glassware and glassblowing equipment just as much as on the transfer of embodied skills.

It was from Wöhler that Liebig learnt of Berzelius' intention to attend the German *Naturforschersammlung* in Hamburg in September 1830, with the result that Liebig decided he must go there to meet him.[607] This meeting is well known but I claim that it acquires a new significance in the context of the *glassware revolution*. Given Berzelius' status as an expert glassblower and innovator of chemical glassware, it seems unlikely to be merely a matter of coincidence that Liebig began the intense programme of analyses during which he developed the *Kaliapparat* immediately following his return from Hamburg. Moving the entire experimental system for combustion analysis into homemade glassware – as Berzelius had done in 1814 – offered significant practical advantages and Liebig, though he never became expert, was certainly sufficiently competent in working glass to take advantage of this strategy. Such a move, moreover, was neither new in itself nor out of step with the current practice of chemistry outside a small number of *élite* laboratories. It also had the potential to solve some of the problems Liebig was probably encountering in attempting to teach his students how to perform organic analyses. Partly because it would be considerably cheaper and available in larger quantities, apparatus made by glassblowing might make it possible to carry out the very large numbers of analyses Liebig was beginning to see would be necessary to tackle the problem of organic analysis. Liebig's solution to the gravimetric determination of carbon during combustion analysis was skilful and ingenious, but it should no longer appear mysterious to us that he sought this solution by blowing and bending small pieces of glass tubing.

## Glassblowing the *Kaliapparat* across Europe

> *When bulbs are to be formed in complicated apparatus, it is good to reflect a little on the best means of effecting the object. It is easy to understand that contrivances which may appear very simple on paper, present difficulties in the practical execution which often call for considerable management.*
>
> *Ferdinand Danger, in John Griffin's English edition (1831)*[608]

In this section, I argue that spreading the use of the *Kaliapparat* was an important part of the means by which chemical glassblowing travelled across Europe. During the early 1830s, the *Kaliapparat* was adopted by chemists in all the main centres of

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[607] Liebig to Wöhler, August 1830, in Lewicki 1991, 1.
[608] Danger 1831, 46.

European chemistry well before it could be acquired from local suppliers of chemical apparatus. Chemists, moreover, did not learn how to use – or indeed how to make – this new piece of glass apparatus from the 1831 paper in which Liebig first introduced it. Many chemists, including Wöhler, acquired this knowledge by personal contact. Liebig, his students and assistants not only demonstrated the use of the *Kaliapparat* but also – at least in the case of Karl Ettling – its production from plain tubes by glassblowing.[609] It is likely that many of these chemists already had some skill in glassblowing but we know of only one case, that of Berzelius, where the receipt of a sample *Kaliapparat* alone was sufficient to enable him to blow his own copies of the new apparatus and, presumably, to use it.[610]

Making a usable *Kaliapparat* without some guidance in how to approach its construction was not easy. For one thing, blowing perfectly spherical glass bulbs was generally recognised to be one of the most difficult basic glassblowing operations.[611] The construction of the *Kaliapparat* required the production of five such bulbs of specific dimensions in addition to multiple tube joining and bending operations. According to Danger (see epigraph), ordering these steps into a workable sequence simply by examining an object would not be straightforward, demanding considerable skill and experience on the part of the glassblower. In the period before the *Kaliapparat* could be obtained as a standard item of chemical apparatus from any reputable supplier, therefore, at least one person in each laboratory using the *Kaliapparat* had to be able to make it by glassblowing. Even those who possessed quite considerable skill in basic glassblowing operations would have found this difficult without knowing how to order the necessary steps, and this helps to explain the geographically limited spread of the *Kaliapparat* in the years before written instructions containing this information became available.[612]

Liebig did not publish instructions for the construction and use of the *Kaliapparat* until 1837, by which time the method of organic analysis using the *Kaliapparat* was in widespread use across Europe. Usselman *et al.* proposed that the design of the *Kaliapparat* had already been modified from Liebig's original construction by his assistant Karl Ettling and it therefore seems likely that the 1837 glassblowing

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[609] Brock (1997, 50) and Brock and Stark (1990, 140) described Ettling's demonstration of how to make a *Kaliapparat* at the 1834 BAAS meeting in Manchester.
[610] Rocke 2003, 98; Usselman *et al.* 2005, 48; Jackson 2006, 288.
[611] See, for example, Danger 1833, 25; Körner 1831, 52.
[612] I have explored this question more extensively in Jackson 2006.

instructions were due, at least in part, to Ettling.[613] These instructions explained how to produce a *Kaliapparat* from glass tubing by following a specified sequence of glassblowing operations. The steps were illustrated with clear diagrams (Figure 9) and, when reproduced in Gregory's English translation (Figure 10) they included a life-size diagram of the completed article. There was, however, no discussion of the glassblowing techniques to be used, suggesting that Liebig considered these to be completely standard.

These instructions, however, are not the earliest published description of how to make a *Kaliapparat*. In 1833 the *Annalen der Pharmacie*, then co-edited by Liebig, reprinted an article written by a French glassblower Lafond and "improved" by Danger entitled *On the Art of Blowing Glass*.[614] The article, which was extracted from the *Journal des Connaissances Usuelles*, presented an introduction to the basic techniques of glassblowing and concluded by providing instructions on how to produce specific items of apparatus. "Since", in the view of the anonymous German translator, "these would be interesting to only the smallest number of chemists and pharmacists", the original items of apparatus had been replaced by Berzelius' washing apparatus and "Herrn Prof. Liebig's apparatus for organic analysis".[615]

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[613] Usselman et al. (2005, 12) proposed that Ettling had reduced the size of the *Kaliapparat* and adjusted its shape so that it could be weighed more easily.
[614] Lafond 1833, 298-313.
[615] Ibid., 312.

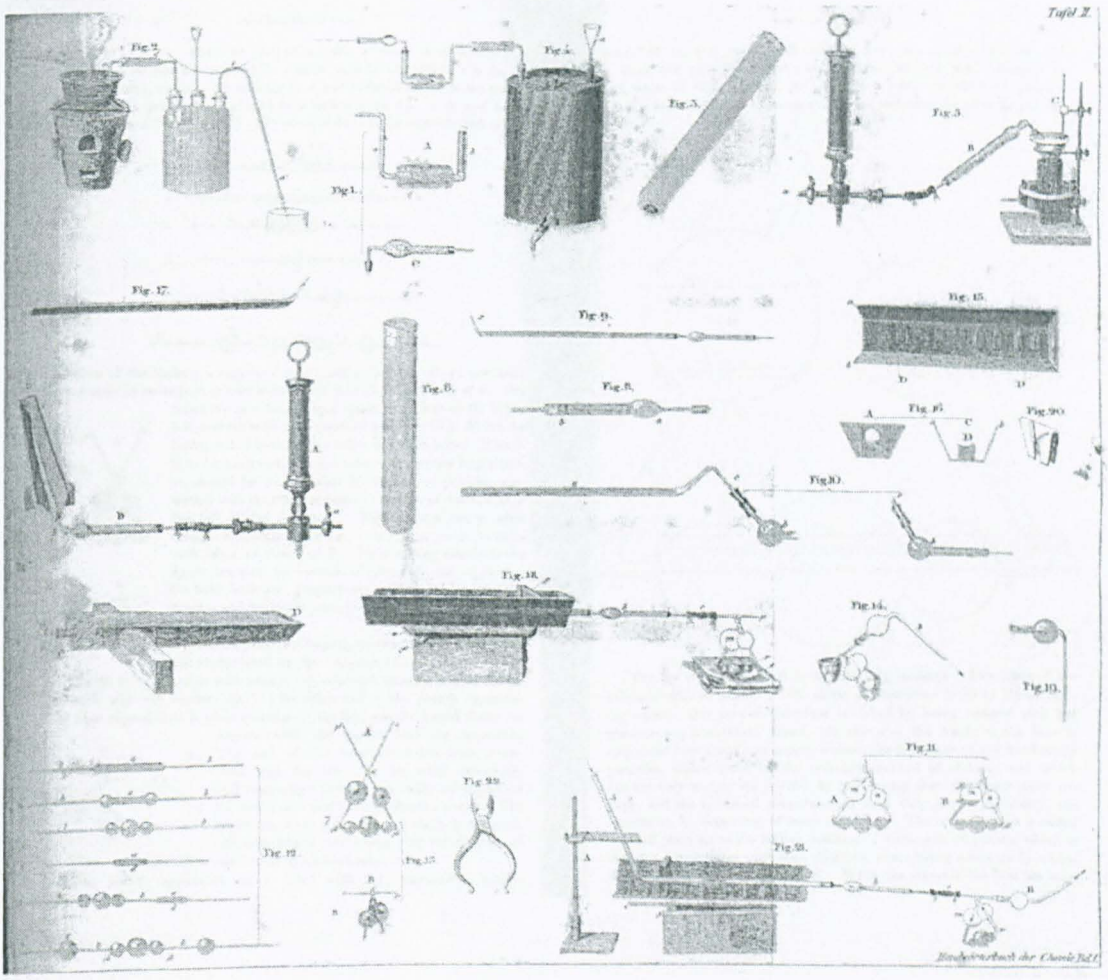
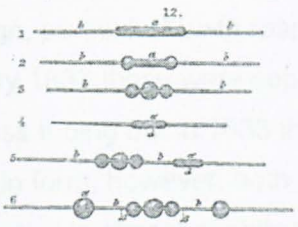


Figure 9. Liebig's (1837) *Anleitung* was richly illustrated, including a series of pictures showing how to produce a *Kaliapparat* by glassblowing (*Figs. 12 and 13*), as well as its incorporation within the combustion apparatus as a whole (*Figs. 18 and 21*).

shape of No. 3. About an inch of a tube, *a*, equal to *a*, is now soldered to a narrow barometer tube similar to *b b*; one end of *a* is drawn out to a point, which is cut off near to *d*, and soldered to one of the points *b*—which is previously reduced to 2 inches (No. 5). *a* is now to be blown out to a bulb, (No. 6.) The same is done at the opposite end of *a*.

12.



One of the bulbs *a a* may be rather smaller than the other; one however must be so large as to hold more liquid than the middle bulb of *a*. The tubes are now heated by a spirit-lamp close to the bulbs, *β β*, and are bent at an angle of 45° (*fig.* 13.) Above the bulbs, *m* and *n*, these two tubes are again bent. Here it is to be observed, that the tube *o*, having the larger bulb *m*, should be so bent that its horizontal portion, connected with the tube containing chloride of calcium, is to the left of the operator. The tubes *o* and *p*, after being sufficiently heated at *a*, are bent so as to cross each other, as shown at B. By attending closely to the figure, we may be certain of giving to the apparatus the best form and proportions. The sharp ends of the tubes *o* and *p* must be rounded in the flame of the spirit-lamp.

13.

[The Apparatus thus prepared has the exact form and size represented by *fig.* 14, page 11.—W. G.]

To fill this apparatus with caustic ley, one end must be connected by a cork with the sucker, *fig.* 15; the other end of the potash apparatus is then dipped into a glass containing the ley, and the liquid drawn by suction with the mouth into the apparatus.

15.

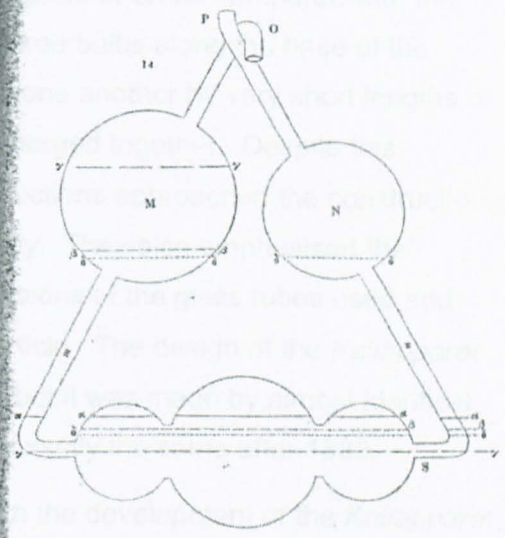
The end of the tube which has been moistened with the ley is to be dried externally, and internally: the latter is easily accomplished by means of a small roll of filtering paper. The apparatus, when quite dry and clean, is weighed, and then joined to the tube with the chloride of calcium by means of a small tube of caoutchouc.

The potash apparatus, when filled with ley, commonly weighs



from 750 to 900 grains. If the ley have the sp. gr. 1.25 to 1.27, it does not produce foam when bubbles of gas pass through it; and when of this strength, its absorptive power is likewise greatest. Caustic soda ley foams like soap and water, and must therefore be avoided.

14




[The ley is best prepared in the following manner. Two parts of the subcarbonate of potash of the shops are dissolved in 20 to 24 of boiling water. One part of quicklime is slaked by being *covered* with hot water in any convenient vessel. In this way the whole of the lime is converted into a uniform cream, without the formation of any hard sandy particles, which occur in the ordinary method of slaking, and which are not only useless but hurtful, by preventing, from the space they occupy, and the increased proportion of lime they render necessary, the separation, by decanting, of much of the ley. The cream of lime is added in small portions to the boiling solution of carbonate of potash, which is boiled a few minutes after each addition, water being occasionally added to supply the loss by evaporation. When the whole of the lime has been

Figure 10. Gregory's (1839) translation of Liebig's (1837) textbook reproduced the same illustrations, but showed the finished *Kaliapparat* at life-size.

It is interesting to compare the description of how to make a *Kaliapparat* which followed (Figure 11) with that published in 1837. One difference is immediately apparent: the form of the *Kaliapparat* in 1833 is rather crude compared with the 1837 design, particularly with respect to the three bulbs along the base of the triangle. By 1837 these were separated from one another by very short lengths of narrow glass tubing but in 1833 they almost merged together. Despite this difference in form, however, both sets of instructions approached the construction of the *Kaliapparat* in almost exactly the same way. They also emphasised the *Kaliapparat*'s correct size by giving the dimensions of the glass tubes used and providing a life-size diagram of the finished article. The design of the *Kaliapparat* was slightly refined between 1833 and 1837, but it was made by almost identical glassblowing methods and its size remained exactly the same after 1833.

These instructions provide a new fixed point in the development of the *Kaliapparat*, showing that whatever modifications were made between late 1830 and early 1883, its design and method of construction were fixed by 1833. Liebig certainly approved the translation of the original article from French into German, and he probably suggested the inclusion of instructions for how to make a *Kaliapparat.* Moreover, it seems reasonable to infer from the manner in which the author referred to Liebig that these instructions were written by one of his students or assistants, the most likely candidate being Ettling. In 1833, shortly after the publication of Blanchet and Sell's key paper establishing a stable method for producing reliable analytical results using the *Kaliapparat*, Liebig began to take steps to enable those outside his sphere of contact to create his new apparatus for themselves.

This certainly marks an important step in the dissemination of the method of analysis using the *Kaliapparat*, but I want to place it in the more general context of the development of chemical glassware, particularly in Germany. In 1833 it did not make sense to publish instructions for how to make a *Kaliapparat* without including a general guide to chemical glassblowing. The translation of Lafond and Danger's article is a very early example of such a text in German, published in the same year as (and probably slightly before) the German translation of Danger's *Art of Glassblowing* and at a time when many German chemists lacked glassblowing skill. Increasing the geographical dispersal of the *Kaliapparat* beyond major centres of chemical research, which was necessary to achieve the standardisation of analytical approach Liebig longed for, could only be achieved by encouraging more chemists to learn how to make chemical glassware and printed instructions offered an

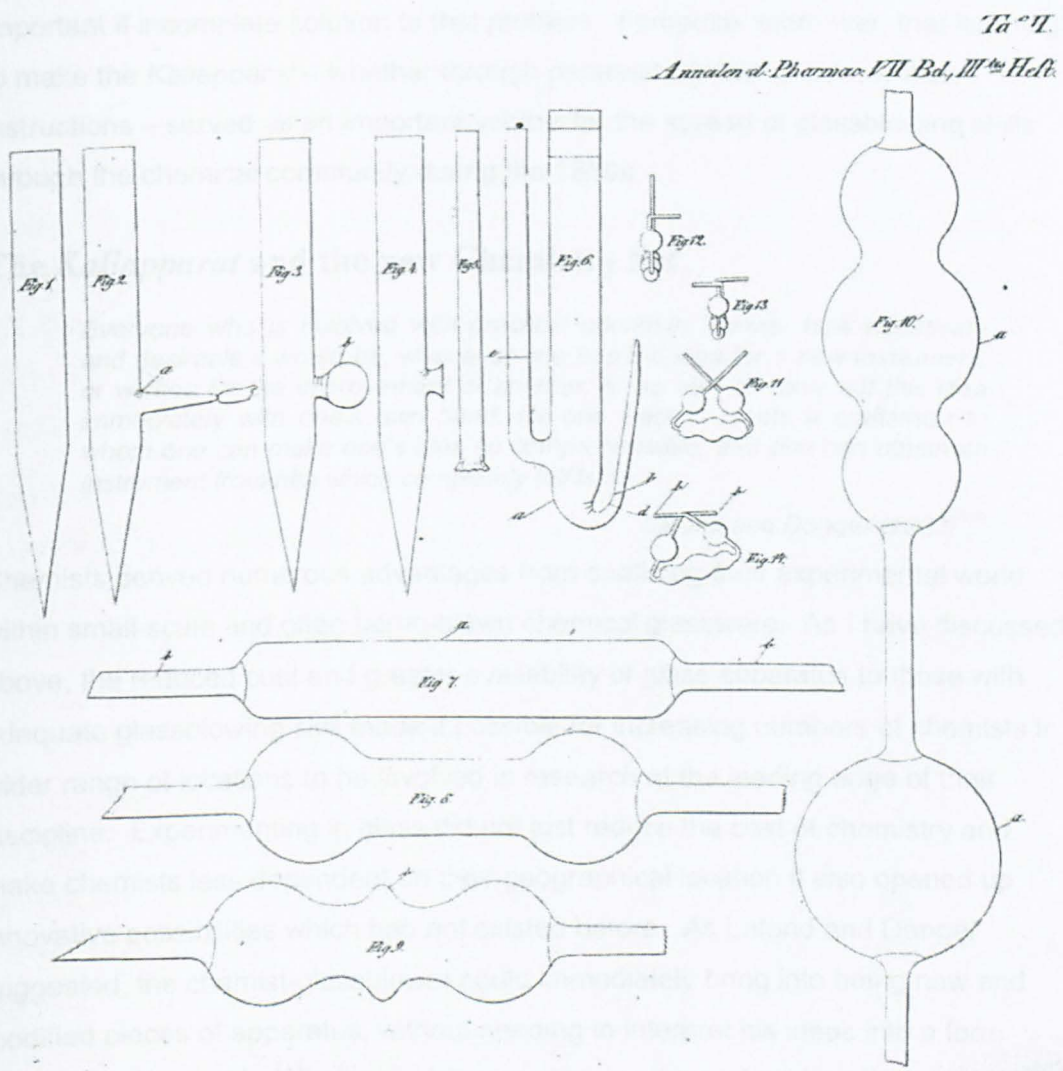



Figure 11. Lafond (1833) included instructions for making a *Kaliapparat* by the same series of glassblowing operations, producing a piece of apparatus which – although of somewhat less polished appearance – was of identical size to the later version.

important if incomplete solution to that problem. I propose, moreover, that learning to make the *Kaliapparat* – whether through personal contact or from written instructions – served as an important vehicle for the spread of glassblowing skills through the chemical community during the 1830s.

## The *Kaliapparat* and the new Chemistry Set

> *Everyone who is involved with practical chemistry knows, how necessary and desirable it would be, whenever one has the idea for a new instrument, or wishes for the improvement of another, to be able to carry out this idea immediately with one's own hand, for one seldom meets a craftsman to whom one can make one's idea so comprehensible, that one can obtain an instrument from him which completely fulfils it.*
>
> *Lafond and Danger (1833)*[616]

Chemists derived numerous advantages from confining their experimental world within small-scale and often home-blown chemical glassware. As I have discussed above, the reduced cost and greater availability of glass apparatus to those with adequate glassblowing skill made it possible for increasing numbers of chemists in a wider range of locations to be involved in research at the leading edge of their discipline. Experimenting in glass did not just reduce the cost of chemistry and make chemists less dependent on their geographical location it also opened up innovative possibilities which had not existed before. As Lafond and Danger suggested, the chemist-glassblower could immediately bring into being new and modified pieces of apparatus, without needing to interpret his ideas into a form someone else could understand. He was able, by virtue of his knowledge of both "the elements, whose unification is involved in the formation of different apparatus" and "the way of combining the individual parts, of which an apparatus consists", to produce a wide variety of apparatus to his own, personal specification.[617]

Exactly this pattern of innovation is displayed in the history of the *Kaliapparat* I describe below, but I also want to draw attention to another consequence of the chemist's increasingly intimate involvement with his apparatus. I will illustrate the design changes chemists introduced to the form of the *Kaliapparat*, some of which achieved general acceptance as improvements on the original design produced by Liebig, but I will also show how chemists began to transfer the *Kaliapparat* into entirely new experimental contexts. By this means, the *Kaliapparat* became dissociated from its original experimental setting within the combustion train of quantitative organic analysis and became much more firmly associated with its

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[616] Lafond 1833, 298.
[617] Ibid., 298-299.

particular function, in this case the complete absorption of a gas when it was passed through a *Kaliapparat* filled with a suitably chosen liquid. I argue that this association of a particular item of chemical glassware with a particular function had important consequences because it enabled chemists to construct carefully controlled and highly visible experimental spaces within which to carry out complex sequences of chemical operations. As my study of Ladenburg's synthesis of coniine will illustrate, this ability – applied to processes of purification, identification and transformation – became an essential aspect of the practice of constructive synthesis.

Examining Griffin's 1866 catalogue *Chemical Handicraft* reveals an entire page devoted to various forms of "Apparatus for the Absorption of Gases by Liquids" (Figure 12).[618] "Liebig's Apparatus for the absorption of Carbonic Acid in a solution of caustic potash" – which Griffin had been supplying since 1841[619] – was the first item, but the catalogue also included several modified versions of the *Kaliapparat*. Will and Varrentrapp's apparatus "for the collection of Ammonia Gas in Hydrochloric Acid" had been developed for the gravimetric determination of nitrogen in quantitative organic analysis, but the versions of Liebig's "potash apparatus" developed by the expert glassblower Heinrich Geissler of Bonn, and by the Professor of Chemistry in Berlin Eilhard Mitscherlich, had been designed for exactly the same purpose as the original *Kaliapparat*. Griffin's catalogue explained that Geissler's apparatus was "so formed as to stand steadily on 3 bulbs", but gave no indication as to why one might prefer Mitscherlich's apparatus over Liebig's original. Griffin described the glassware and furnaces required for quantitative organic analysis elsewhere in this catalogue, but there was nothing on this page to suggest that these small, curiously shaped, and yet relatively inexpensive items of glassware were intended for that purpose. By 1866, the *Kaliapparat* and its offspring had become generic items, classified by their gas-absorbing *function* and no longer associated exclusively with the original *context* of their development, quantitative organic analysis.

In the field of organic analysis, and much to Liebig's *chagrin*, Mitscherlich's adaptation of the *Kaliapparat* became the first choice of many analysts. Mitscherlich learnt to use the *Kaliapparat* directly from Liebig, and the two published a joint

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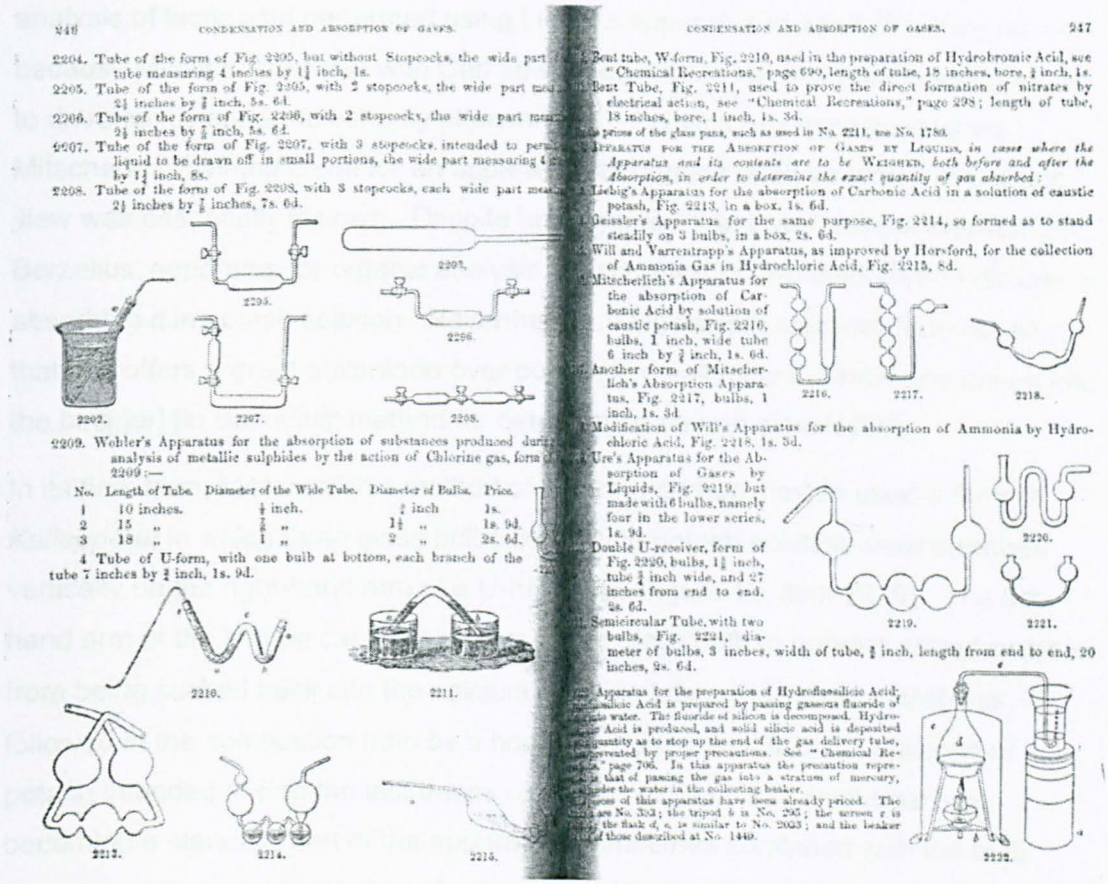
[618] Griffin 1866, 247. The frontispiece illustration of this catalogue showed Griffin's combustion furnace containing a combustion train fitted with Will and Varrentrapp's apparatus for the absorption of ammonia.
[619] Griffin 1850, Part I, July 1841, p. 37.



246 CONDENSATION AND ABSORPTION OF GASES.

2204. Tube of the form of Fig. 2205, but without Stopcocks, the wide part of tube measuring 4 inches by 1¼ inch, 1s.

2205. Tube of the form of Fig. 2205, with 2 stopcocks, the wide part measuring 2½ inches by ¾ inch, 5s. 6d.

2206. Tube of the form of Fig. 2206, with 2 stopcocks, the wide part measuring 2½ inches by ¾ inch, 5s. 6d.

2207. Tube of the form of Fig. 2207, with 3 stopcocks, intended to permit liquid to be drawn off in small portions, the wide part measuring 4 inches by 1¼ inch, 8s.

2208. Tube of the form of Fig. 2208, with 3 stopcocks, each wide part measuring 2½ inches by ¾ inches, 7s. 6d.

2202. 2207. 2208. 2209. 2206.

2209. Wohler's Apparatus for the absorption of substances produced during analysis of metallic sulphides by the action of Chlorine gas, form of 2209:—

| No. | Length of Tube. | Diameter of the Wide Tube. | Diameter of Bulbs. | Price. |
|---|---|---|---|---|
| 1 | 10 inches. | ½ inch. | ¾ inch | 1s. |
| 2 | 15 „ | ¾ „ | 1¼ „ | 1s. 9d. |
| 3 | 18 „ | 1 „ | 2 „ | 2s. 6d. |

4 Tube of U-form, with one bulb at bottom, each branch of the tube 7 inches by ¾ inch, 1s. 9d.

2210. 2211.

2213. 2214. 2215.

CONDENSATION AND ABSORPTION OF GASES. 247

Bent tube, W-form, Fig. 2210, used in the preparation of Hydrobromic Acid, see "Chemical Recreations," page 690, length of tube, 18 inches, bore, ¾ inch, 1s.

Bent Tube, Fig. 2211, used to prove the direct formation of nitrates by electrical action, see "Chemical Recreations," page 298; length of tube, 18 inches, bore, 1 inch, 1s. 3d.

Prices of the glass pans, such as used in No. 2211, see No. 1780.

APPARATUS FOR THE ABSORPTION OF GASES BY LIQUIDS, *in cases where the Apparatus and its contents are to be* WEIGHED, *both before and after the Absorption, in order to determine the exact quantity of gas absorbed:*

Liebig's Apparatus for the absorption of Carbonic Acid in a solution of caustic potash, Fig. 2213, in a box, 1s. 6d.

Geissler's Apparatus for the same purpose, Fig. 2214, so formed as to stand steadily on 3 bulbs, in a box, 2s. 6d.

Will and Varrentrapp's Apparatus, as improved by Horsford, for the collection of Ammonia Gas in Hydrochloric Acid, Fig. 2215, 8d.

Mitscherlich's Apparatus for the absorption of Carbonic Acid by solution of caustic potash, Fig. 2216, bulbs, 1 inch, wide tube 6 inch by ¾ inch, 1s. 6d.

Another form of Mitscherlich's Absorption Apparatus, Fig. 2217, bulbs, 1 inch, 1s. 3d.

Modification of Will's Apparatus for the absorption of Ammonia by Hydrochloric Acid, Fig. 2218, 1s. 3d.

Ure's Apparatus for the Absorption of Gases by Liquids, Fig. 2219, but made with 6 bulbs, namely four in the lower series, 1s. 9d.

Double U-receiver, form of Fig. 2220, bulbs, 1¼ inch, tube ¾ inch wide, and 27 inches from end to end, 2s. 6d.

Semicircular Tube, with two bulbs, Fig. 2221, diameter of bulbs, 3 inches, width of tube, ¾ inch, length from end to end, 20 inches, 2s. 6d.

Apparatus for the preparation of Hydrofluosilicic Acid. Fluosilicic Acid is prepared by passing gaseous fluoride of silicon into water. The fluoride of silicon is decomposed, Hydrofluoric Acid is produced, and solid silicic acid is deposited in quantity as to stop up the end of the gas delivery tube, unless prevented by proper precautions. See "Chemical Recreations," page 706. In this apparatus the precaution represented is that of passing the gas into a stratum of mercury, and under the water in the collecting beaker.

The prices of this apparatus have been already priced. The flask is No. 353; the tripod b is No. 295; the screen c is No. 2023; the flask d, e, is similar to No. 2023; and the beaker is one of those described at No. 1449.

2216. 2217. 2218. 2219. 2220. 2221. 2222.

Figure 12. Griffin's (1866) *Chemical Handicraft* contained an entire page devoted to various forms of "Apparatus for the Absorption of Gases by Liquids". Mitscherlich's apparatus (*Item 2216*)

analysis of lactic acid performed using Liebig's apparatus in 1833.[620] They fell out because Mitscherlich sided with Carl Löwig against Liebig, and Mitscherlich began to develop his apparatus shortly afterwards.[621] Liebig's fury increased when Mitscherlich claimed credit for an apparatus for organic analysis which in Liebig's view was essentially his own. Despite his assertion that it was almost identical to Berzelius' apparatus for organic analysis, Mitscherlich determined carbon dioxide by absorbing it in potash solution. Nevertheless, Mitscherlich claimed, "I do not see that this offers a great advantage over potash in small pieces, which one brings into the bell[-jar] [in Berzelius' method for determining carbon dioxide]".[622]

In its final form, Mitscherlich's method of trapping carbon dioxide used a form of *Kaliapparat* in which three glass bulbs containing potash solution were arranged vertically on the right-hand arm of a U-tube (see Figure 12, item 2216). The left hand arm of the U-tube carried a single, larger glass bulb to prevent potash solution from being sucked back into the calcium chloride tube. This *Kaliapparat* was followed in the combustion train by a horizontal glass tube filled with pieces of potash intended to trap the last traces of carbon dioxide, this additional tube becoming a standard part of the apparatus, sometimes combined with the bulb apparatus into a single piece of glassware.[623] Mitscherlich's letters to Berzelius during this period show that he was concerned that the values he obtained for carbon during the analysis of fats and oils were invariably too low as a result of incomplete combustion.[624] As well as flushing the apparatus with oxygen after the combustion, Mitscherlich took precautions to ensure that all the carbon dioxide was being trapped (and that no water was being lost from the *Kaliapparat*). It was at Berzelius' suggestion that he introduced the second tube containing solid potash, and he reported to Berzelius in June 1838 that this tube had gained from 0.004 to 0.005 g during the combustion of stearic acid.[625] Although Liebig's *Kaliapparat* was sufficiently accurate for most analyses, Mitscherlich found this not to be the case for substances with relatively high molecular weight such as fatty acids whose carbon content was particularly large.[626]

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[620] Mitscherlich and Liebig 1833, 47-48.
[621] Liebig to Berzelius, 25 March 1834, in Lewicki 1991, 84.
[622] Mitscherlich to Berzelius, June 1834, in Mitscherlich 1896a, 108.
[623] Mitscherlich 1896b, 449 and 1837, 125-148.
[624] Mitscherlich to Berzelius, 10 June 1838, in Söderbaum 1937, 248.
[625] Mitscherlich to Berzelius, June 1838, in Söderbaum 1937, 251.
[626] Liebig hotly disputed the need for this modification to the *Kaliapparat* (in correspondence with Berzelius), but the widespread adoption of Mitscherlich's apparatus suggests that there

Mitscherlich's adaptation of the *Kaliapparat* seems to have improved the accuracy of carbon determination, which was important for the analysis of certain classes of substance. It also incorporated a much larger first bulb intended to prevent the failure of analyses as a result of suck-back through the combustion train, a feature that must have benefited inexperienced analysts. Mitscherlich's *Kaliapparat* was also of rather simpler construction in glassblowing terms, with the result that it could be made more easily by chemists, and sold at a lower price by suppliers of chemical glassware. Geissler's "potash bulbs", by contrast, may have offered some handling advantages during weighing, but their more complicated construction led to a considerably higher selling price (2s. 6d. in 1866, compared with 1s. 6d. for Liebig's *Kaliapparat*) which was probably off-putting to some chemists, particularly when large numbers were needed for teaching.

By the end of the century, the catalogue of Charles Gerhardt's Bonn firm offered no fewer than nine variants of Liebig's original *Kaliapparat* (Figure 13), including those introduced by Geissler and Mitscherlich.[627] Mitscherlich's apparatus – which now typically consisted of four bulbs vertically connected following the first, larger bulb – was offered with and without the additional potash tube suggested by Berzelius. Geissler's apparatus was offered in three variations, one of which included 5 bulbs along the base rather than the usual three. Two of these bulbs, which were separable from the rest, were intended to contain sulphuric acid, presumably as a drying agent. Several of the *Kaliapparate* offered by Gerhardt had been designed to stand on a flat surface, including Kyll's curious modification of Liebig's apparatus in which the middle of the three bulbs along the base was blown in the shape of a prism. Gerhardt's catalogue also contained Dittmar's modification of Liebig's *Kaliapparat*, in which the fifth bulb was designed to function as a washing flask (and so to improve the absorption of gas). In the almost seventy years since Liebig's introduction of the *Kaliapparat*, chemists throughout Europe had not simply adopted it in its original form and for its original purpose. Some of their modifications – for example those that made the *Kaliapparat* able to stand unsupported – increased its ease of use and meant that it could be weighed on un-adapted pan balances. Others – such as Dittmar's – were designed to improve its performance to suit their own particular purposes, many of which were by now far removed from the

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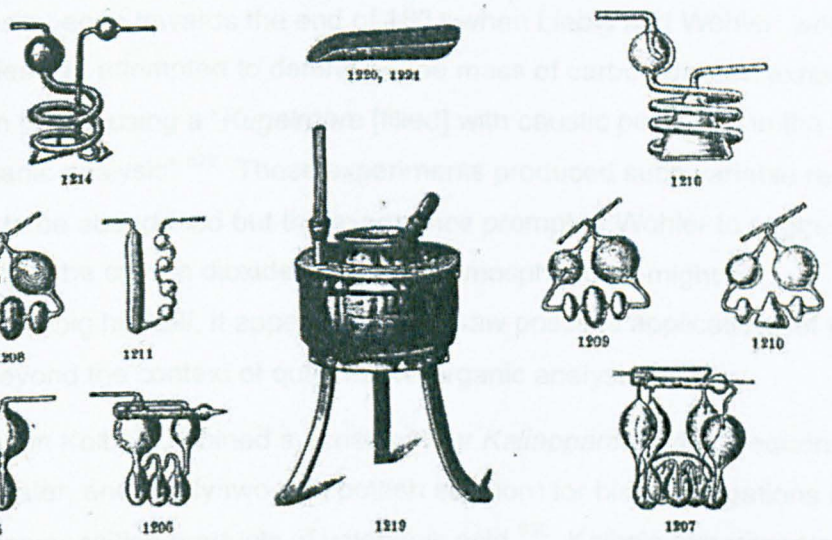
were circumstances in which the original *Kaliapparat* was insufficiently accurate to determine the number of carbon atoms.

[627] Gerhardt 1898, 95. As far as I can establish, the instrument manufacturer was not related to the chemist.




C. Gerhardt, Marquart's Lager chemischer Utensilien, Bonn.

*1205 Kaliapparat nach Geissler, in Pappkästchen . . . . . Mark 1.05
*1206 — mit angeschliffener Kaliröhre . . . . . „ 2.20
*1207 — derselbe, verändert von Dr. A. Vandenberghe, mit 5 Kugeln, 2 enthalten Schwefelsäure und sind abnehmbar (Chem.-Ztg. XIX 1895, S. 877) Mark 3.—
*1208 — nach Liebig, in Pappkästchen . . . . . „ 1.—
*1209 — nach Liebig, verändert von Dittmar; die fünfte Kugel ist, um als Waschflasche zu arbeiten, mit eingeblasener, knieförmig gebogener Röhre versehen (Chem.-Ztg. XII, 1888, S. 1555) . . . . . Mark 1.25
*1210 — nach Liebig, verändert von Kyll, stehend . . . . . „ 1.—
*1211 — nach Mitscherlich, verändert von de Koninck . . . „ 1.—
1212 — nach Mitscherlich, mit angeschliffener Kaliröhre und mit Füsschen zum Stehen. . . . . Mark 2.20
1213 — nach Schiff, stehend (Fresenius' Zeitschrift 1889, S. 679) „ 9.—
*1214 — Schlangenapparat nach Winkler . . . . . „ 1.50
1215 — derselbe mit angeschliffener Kaliröhre . . . . . „ 2.50
*1216 — derselbe, verändert von Kyll . . . . . „ 1.50
1217 Kalibermass von Buchsbaumholz, zum Messen des äusseren Durchmessers von Röhren u. dergl. bis zu 80 Millimeter, in Millimeter getheilt, Mark 1.50
1218 — von Metall, vernickelt, mit Nonius und mit Schraube zum Feststellen Mark 4.—
*1219 Kalischmelze, Apparat dazu nach Liebermann (Berichte der deutschen chemischen Gesellschaft 1888, 13, Seite 2528), bestehend aus Schmelzkessel von 130 Mm. Durchm. und 70 Mm. Tiefe und Löffel von reinem



Figure 13. By the end of the century, Liebig's *Kaliapparat* (1208) was merely one – and one of the cheapest – of many variants on the same theme. Gerhardt 1898, 95.

*Kaliapparat*'s original context of development.

The process by which the *Kaliapparat* began to transcend the context of quantitative organic analysis began towards the end of 1831 when Liebig and Wöhler, working together in Giessen, attempted to determine the mass of carbon dioxide exhaled during a given period using a "*Kugelröhre* [filled] with caustic potash ... in the same way as in organic analysis".[628] These experiments produced such variable results that they had to be abandoned but the experience prompted Wöhler to suggest a method by which the carbon dioxide content of atmospheric air might be measured.[629] Liebig himself, it appears, quickly saw possible applications of the *Kaliapparat* beyond the context of quantitative organic analysis.

In 1849 Hermann Kolbe combined a series of four *Kaliapparate* (filled sequentially with alcohol, water, and finally two with potash solution) for his investigations of the electrolytic decomposition products of valerianic acid.[630] Kolbe's experiments were intended to lead to "important conclusions about the chemical constitution of organic compounds".[631] Kolbe hypothesised that acetic acid was composed of oxalic acid with methyl, which he anticipated would be split on electrolysis. When, however, his preliminary experiments showed that acetic acid did not produce the expected results, Kolbe eventually settled on valerianic acid as the most straightforward subject for his investigations.[632] Kolbe isolated a clear, colourless liquid with constant boiling point 108° C, which he named *valyl*,[633] and a gas which he declared to be "identical" with *ditetryl* which had first been prepared by Faraday and later named by Berzelius.[634] By reacting this gas with chlorine, Kolbe produced a chloride whose boiling point of 123° C agreed well with the value he predicted for "Chlorditetryl = $C_8H_8Cl_2$" using work on boiling point regularities by Hermann Kopp and Charles Gerhardt.[635] When he repeated this procedure with acetic acid, Kolbe filled one *Kaliapparat* in his apparatus with sulphuric acid to ensure that the gas he

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[628] Wöhler to Berzelius, 1 December 1831, from Wallach 1901, 385-387: 386.
[629] According to Wallach (1901, fn. pp. 386-387) an experiment of the kind recommended by Wöhler was performed by Brunner.
[630] Kolbe 1849, 269. See also Figure 1 referred to therein.
[631] I note *apropos* the argument in Chapter 3 that this work was discussed by Partington (1964, 504-505) under the heading "Kolbe's Syntheses".
[632] Kolbe 1849, 258.
[633] In his quantitative analysis of *valyl*, Kolbe (1849, 264 and fn.) noted both the difficulty of ensuring its complete combustion, and his use of an additional tube containing melted potash to ensure the absorption of any water carried from the potash solution in the *Kaliapparat* by the stream of air, i.e. Mitscherlich's modification.
[634] Kolbe 1849, 273. *Ditetryl* later became known as isobutylene. See Partington 1964, 108.
[635] Ibid., 277-278.

collected was free from water and other impurities.[636] He obtained carbon dioxide and a substance he identified as *methyl*, which tended to confirm his views on the constitution of acetic acid, but inconsistencies in his quantitative results prevented him from drawing any firm conclusion.[637]

Kolbe's experiments were inconclusive with regard to his original goal of improving knowledge of the constitution of acetic acid but the apparatus he described and illustrated became a model for other chemists investigating the gaseous products of the decomposition of organic substances. Although it included various standard elements such as the gasometer, "[a]bout whose purpose and arrangement exhaustive instructions are to be found ... in [Poggendorff's] chemical dictionary", Kolbe's "system of tubes" consisted largely of a novel combination of simple glassware elements.[638] Kolbe – who had carried out these experiments in the laboratories of Lyon Playfair in London and Robert Bunsen in Marburg – put the *Kaliapparat* to work in a new way by filling it with liquids other than potash and by combining four *Kaliapparate* in sequence, but his apparatus also exemplifies chemists' ability to construct original and increasingly complex experimental spaces from readily available, standard items of glassware.

Kolbe's use of the *Kaliapparat* could be adapted to the study of other gaseous decomposition products. In the early 1880s, for example, Ladenburg used "two Liebig's *Kugelröhren* and a gasometer" in his investigation of the decomposition of tropine by soda lime.[639] The first *Kaliapparat* contained dilute hydrochloric acid, which removed bases as their hydrochloride salts; the second, containing bromine, trapped traces of an organic bromide containing 69.1% bromine.[640] In applying Kolbe's experimental approach, Ladenburg was able to decide how many *Kaliapparate* were needed and what absorbing liquids they should contain. The possibility of combining individual glassware components at will introduced a new flexibility into the design of chemical apparatus which did not necessarily entail the bespoke production of particular items of glassware. Even where they made use of existing pieces of glassware, chemists could apply their knowledge of a particular

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[636] Ibid., 290.
[637] Ibid., 293.
[638] Ibid., 269. Kolbe referred in a footnote (p. 270) to his (1848) entry on the collection and storage of gases in Poggendorff's *Handwörterbuch*.
[639] Chemists have used a wide variety of terms to denote the piece of glassware introduced by Liebig (1831b). Except where direct quotation requires otherwise, I have used only *Kaliapparat*.
[640] Ladenburg 1883b, 115.

chemical process to construct the most appropriate apparatus from standard components such as the *Kaliapparat*.

The *Kaliapparat* continued to find new applications in analytical chemistry throughout the nineteenth century. In 1891, for example, the analytical chemist George McGowan, who had studied with Kolbe in Leipzig, published a new apparatus for the estimation of nitric acid in nitrates which incorporated "a Geissler bulb apparatus" in Dittmar's modification.[641] The basis of this method was the quantitative production of nitrosyl chloride and chlorine from the reaction of nitrates with concentrated hydrochloric acid. Passing these gases through potassium iodide liberated iodine "exactly equivalent to the *whole* of the chlorine present (free and combined)", and the iodine could then be titrated in the usual manner with sodium thiosulphate. It was, McGowan continued, "absolutely essential" to exclude air from the apparatus (Figure 14), which was "very simple, and can readily be made by any one moderately expert at glass-blowing."[642] McGowan's apparatus incorporated a condenser – "a simple tube, slightly enlarged at the foot into two small tubes" – and a "Geissler bulb apparatus" (*Kaliapparat*) filled with potassium iodide solution. The primary function of the *Kaliapparat* was to ensure complete absorption of chlorine, but it also provided visual feedback to help the analyst regulate the process. As McGowan explained, "The Geissler bulbs should be so arranged that gas only bubbles through the last of them, the liquid in the others remaining quiescent".[643]

McGowan provided detailed instructions for the execution of the analysis, explaining that "very little practice enables the operator to judge as to the proper rate of warming" of the reaction with hydrochloric acid, by watching the flow of bubbles through the apparatus and noting the colour changes which accompanied reaction. The transparency of the apparatus, which was entirely made of glass components, enabled the analyst to observe what was happening at all points during the analysis, and provided visible evidence to show whether the analysis had been successfully carried out.[644] "At the end of a properly conducted experiment", McGowan explained, "the liquid in the last bulb of the Geissler apparatus ought to be only pale yellow".[645]

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[641] McGowan 1891, 531. "(Dittmar's modification was used)". McGowan 1884a and 1884b were the published output of McGowan's time in Leipzig.
[642] McGowan 1891, 530.
[643] Ibid., 532.
[644] Ibid., 530. McGowan even noted that ground glass stoppers had been used rather than corks or rubber stoppers, both of which would react with chlorine gas.
[645] Ibid., 536.

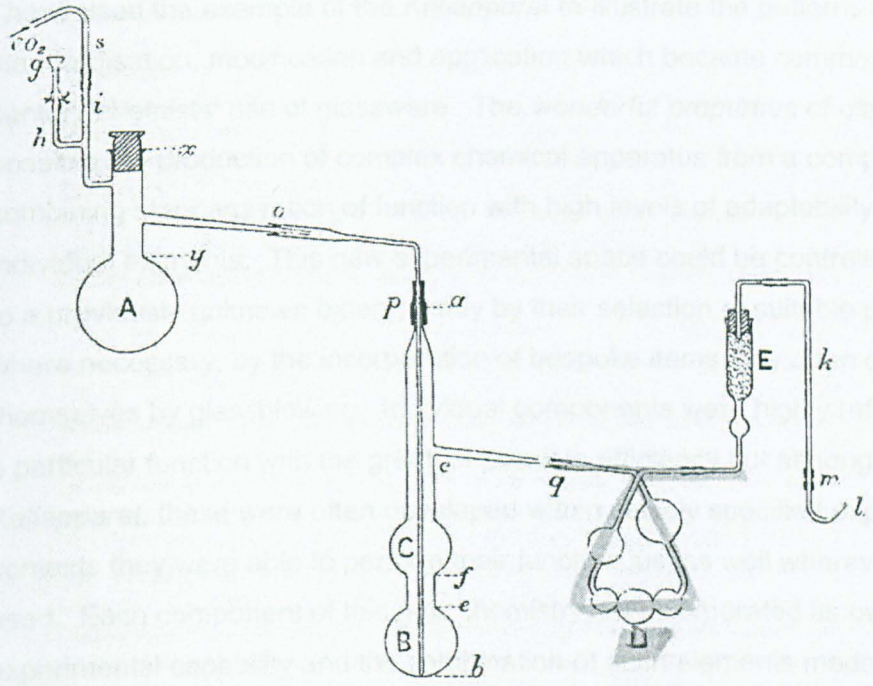


Figure 14. McGowan's apparatus (1891, 531) combined a bespoke condenser (BC) with a *Kaliapparat* in Geissler's modification (D) to trap the chlorine produced in the analysis.

I have used the example of the *Kaliapparat* to illustrate the patterns of innovation, standardisation, modification and application which became common in nineteenth-century chemists' use of glassware. The *wonderful properties of glass* made possible the production of complex chemical apparatus from a component system combining standardisation of function with high levels of adaptability in the design of individual elements. This new experimental space could be controlled by chemists to a previously unknown extent, partly by their selection of suitable parts and also, where necessary, by the incorporation of bespoke items they often created themselves by glassblowing. Individual components were highly refined to perform a particular function with the greatest possible efficiency but although, like the *Kaliapparat*, these were often developed within closely specified experimental contexts they were able to perform their function just as well wherever they were used. Each component of this new chemistry set incorporated its own particular experimental capability and the combination of such elements made it possible for chemists to achieve previously unattainable levels of experimental sophistication.

The chemist's ability to make minute adaptations to both individual components and the experimental train as a whole were important in the precise management of this new space of chemistry. As Danger and Lafond suggested, the chemist-glassblower was not dependent on someone else to interpret his design ideas, which gave him increasingly complete control over the chemical processes he initiated. The ability to work glass, however, was only one of the properties of glass which made it possible for chemists to create this new experimental world. The transparency of glass was just as important, allowing chemists visual access to chemical processes which were often inaccessible to their other senses, confined within closed apparatus. Alchemists might have spent long hours peering into the philosopher's egg, but nineteenth-century chemists obtained much more detailed information concerning the progress and success of their hoped-for reactions by observing streams of bubbles as they passed through liquid, and the various changes of colour which accompanied chemical transformation.

## Constructing Chemical Identity

> *The melting point of the hydrochloride of the synthetic active base was found in Roth's apparatus to be 217°.5, that of coniine from 217°.5 to 218°.5.*
>
> *Herewith is proved the complete identity of coniine with dextrorotatory α-propylpipderidine.*
>
> *Albert Ladenburg (1886)*[646]

In early studies of the newly isolated alkaloid coniine its reported boiling point varied by more than sixty degrees, from 150° C to more than 210° C.[647] Ladenburg's final proof of the identity of his synthetic base – called *dextrorotatory α-propylpipderidine* – with natural coniine, by contrast, rested on determining the melting points of their hydrochloride salts and finding them within one degree of each other (see epigraph). In little over half-a-century chemists had fashioned melting and boiling point into decisive indicators of chemical purity and identity, roles they retained until well into the twentieth century. Because we take the simplicity, uniqueness and stability of these physical characteristics for granted, it is easy to forget that nineteenth-century chemists had to construct accurate, reliable and reproducible measurements of melting and boiling points, and not at all obvious what prompted them to do so.

Chemists had for decades made measurements of this kind whenever they produced new substances, but before the mid-nineteenth century there was little or no expectation that such values should be characteristic. In his 1849 study of coniine, for example, John Blyth concluded that: "Between 168° and 171° C. (335° and 350° F.) may therefore be taken as the nearest approximation to the boiling point of coniine." Blyth noted but expressed no concern that: "Geiger found it to be 150° C. (302° F.), Christison 188° C. (377° F.), and Ortigosa 212° C. (394° F.)." Particularly in the case of complex organic substances, as I discussed in Chapter Three, chemical identity remained intimately bound up with origin until well after 1830. It was no surprise to Blyth that other chemists before him had measured such different values for the boiling point of coniine; on the contrary, it was to be expected. There were few available means of purifying organic substances, especially those that could not be crystallised, with the result that many samples contained impurities derived from the method by which they had been prepared. Even crystalline solids purified by repeated re-crystallisation could rarely be entirely freed of solvent. By reporting the boiling point of his carefully purified and analysed sample, however, I

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[646] Ladenburg 1886a, 2582. The prefix α, like *ortho*, signified the carbon atom next to nitrogen.
[647] Blyth 1849a, 349.

assert that Blyth's work set a new standard for comparison, measured in relation to a defined elemental composition.

In this section I argue that the measurement of characteristic physical properties including boiling (and melting) point was inseparable from a new concept of chemical purity, and that both these factors were essential to the emergence of the chemical identity of a substance as independent of its origins. If chemical purity was at least partly defined by the practice of quantitative organic analysis, moreover, this understanding of independent chemical identity was a fundamental requirement of synthetic organic chemistry. New notions of chemical identity and purity, and their associated characteristic physical properties were, I claim, simultaneously products of and motivating forces for the transition from analytic to synthetic organic chemistry during the mid-nineteenth century.

The nexus of these inter-connections was practical: how was it possible to purify a substance so that its composition and physical properties were meaningful; and how could these attributes be measured sufficiently reliably to serve as characteristics of identity and purity? Certain aspects of the first question have been addressed by histories of techniques such as distillation. We have some idea, for example, that the ancient practice of distillation proved of limited use in separating complex mixtures of organic substances with similar boiling point, this difficulty being largely overcome by the introduction of a glass column below the still head which improved the temperature separation achieved during distillation.[648] The case of distillation, moreover, further illustrates the role of glassware innovation in the development of chemical practice. By the end of the nineteenth century chemists had produced a wide variety of differently formed fractionating columns, all designed in glass to solve particular problems in the practice of distillation.[649] Confronted by the difficulty of obtaining pure pyridine and α-picoline during his attempts to synthesise alkaloids including coniine (described more fully in the following section), Ladenburg developed a new flask which became a standard item of chemical apparatus (Figure 15).[650] Later in the nineteenth century, the introduction of sealed glass distillation apparatus which could be maintained below atmospheric pressure enabled the purification of many non-volatile organic substances which otherwise decomposed

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[648] According to Robert Anderson (2002, 29) the most extensive survey of distillation literature remains Forbes 1970 [1948].
[649] Gattermann 1894, 17-18.
[650] Ladenburg 1888, 3-4; and Fig. 1, Taf. 1.

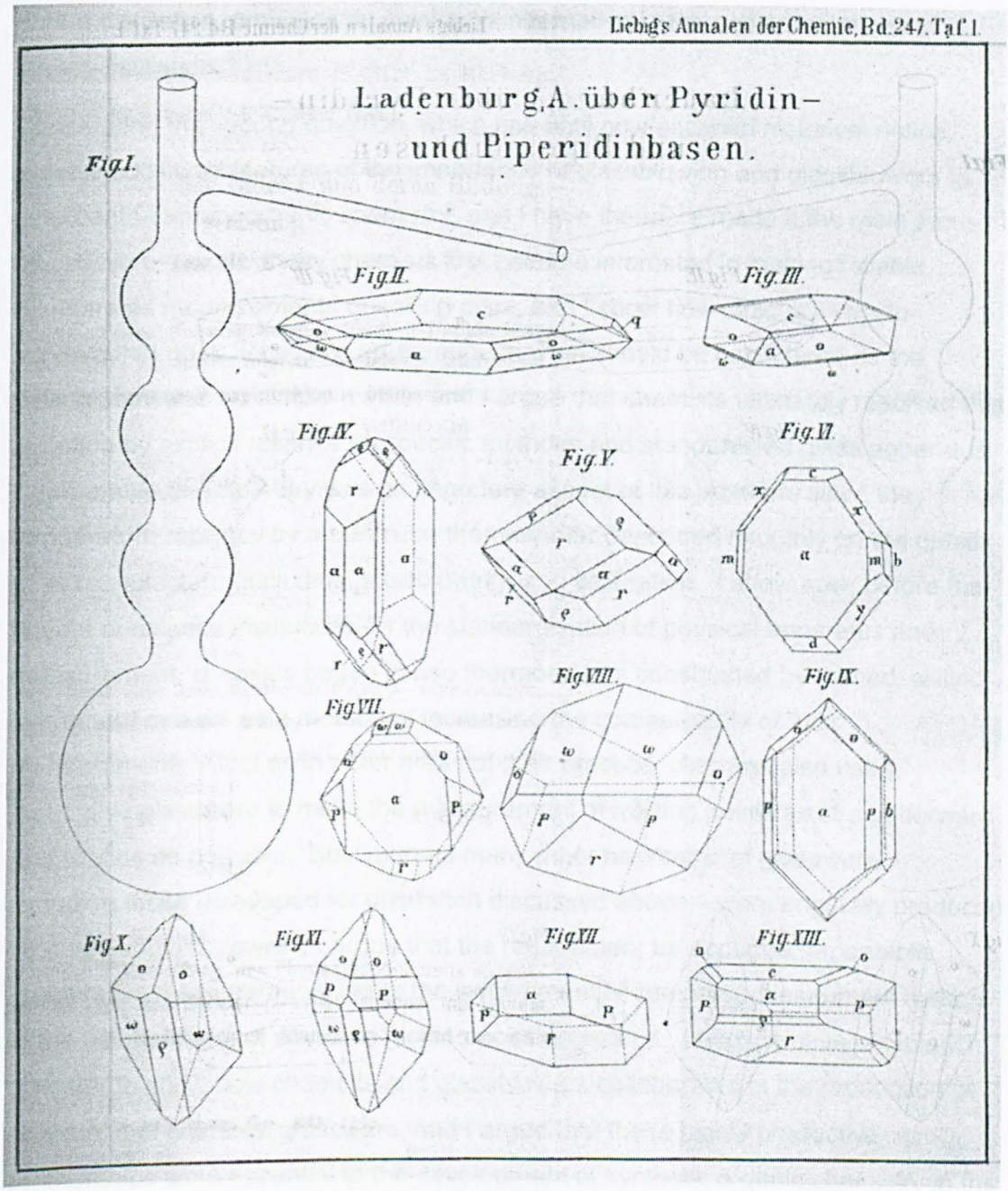


Figure 15. Ladenburg's (1888, Tafel 1) flask combined distillation vessel, fractionating column and still head within a single piece of glassware.

during distillation, providing an invaluable alternative to the earlier technique of steam distillation.[651]

Considering the second question, which has until now escaped historical notice, reveals additional features of the importance of glassblowing and glassblowers to nineteenth-century organic chemistry, and I have therefore made it the main focus of this section. I explain why chemists first became interested in making reliable, comparable measurements of boiling point, and I show how difficult it was to achieve that goal. Reaching agreement on what should be considered as the boiling point was no simple matter, and I argue that chemists ultimately resolved this question by explicit reliance on specific methods and standardised glass apparatus. Comparable thermometry was an important aspect of this problem, since the temperature reported by a particular thermometer depended minutely on the details of its manufacture (including glassblowing) and calibration. I show how, before the advent of national institutions for the standardisation of physical apparatus and measurement, chemists began to use thermometers constructed by named, skilled instrument makers as a method of increasing the comparability of their measurements. Just as in other areas of their practice, chemists also used innovative glassware to make the measurement of melting points as straightforward and routine as possible. But whereas many other new items of glassware – including those developed for distillation discussed above – were originally produced by chemist-glassblowers, I argue that the requirement for accurate, repeatable quantitative measurements led to the involvement of specialised instrument makers in the development of standard melting point apparatus. I use the case of Heinrich Geissler to show how chemists and glassblowers collaborated in the production of new items of chemical glassware, and I argue that these highly productive partnerships were essential to the development of synthetic organic chemistry in the late-nineteenth century.

One of the first chemists who sought to elevate the status of boiling point from peripheral observation to essential characteristic was Hermann Kopp.[652] Kopp was motivated by the wish to demonstrate a law-like relationship between chemical

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[651] This technique relied on vacuum pumps developed around the mid-century by Heinrich Geissler and Hermann Sprengel. See L'Estrange Turner 1992, 103-4; Sprengel 1865. On the development of vacuum distillation see Perkin 1888.

[652] Hermann Kopp, who was *Privatdozent* and later Professor of Chemistry in Giessen during the 1840s, was one of the first to notice the relationship between boiling point and composition of organic substances, which he sought to interpret as a physical law, expressible by a mathematical formula. See Kopp 1844, 71. Kopp's biographical details are taken from Thorpe 1893, and the shorter Thorpe 1896-1897, i-v.

composition and boiling point. He was ultimately unsuccessful, but the debates prompted by his proposal were nevertheless important because they demonstrated a need to standardise such measurements. In 1845, Kopp insisted – against considerable opposition – that, even where they were the express purpose of the investigation, boiling points were "inexact to a certain limit".[653] Kopp's view was largely based on the existence of "different, in themselves equally reliable, results for *the same* substance".[654] In the case of alcohol, "one of the bodies whose boiling point is known most accurately", the boiling points reported by Gay-Lussac, and by Dumas and Boullay differed by more than 2° C, only 0.5° C being explicable by the 15 mm difference in pressure. This, and other similar cases, caused Kopp to question whether "as a rule one ... is entitled to regard each perfectly isolated result for a boiling point as accurate to 1 to 2°".[655] His critics, Kopp lamented, had unfortunately not explained "how one should consider it, when there exist results for the same substance which are *not* in agreement made by two equally good observers".[656]

One aspect of the problem, Kopp explained, was that no attention was generally paid to what kind of vessel was used, or what had previously been contained in it. Elevated boiling points in glass vessels, for example, were known to be obtained if the vessel had previously contained sulphuric acid or alcohol, however well it had been washed out.

> *One could raise the question: if we wish to investigate boiling point regularities, what is then to be regarded as the boiling point? One and the same liquid boils under different conditions at different temperatures, even when the air pressure is the same; which [temperature] is it, for which a dependence on the composition is to be proved? This temperature, the boiling point, is clearly to be regarded only as the one where the tension of the [saturated] vapour of the liquid is equal to the prevailing air pressure. During observations of the boiling point made in the usual way, one easily obtains a too high, an abnormal boiling point.*[657]

Kopp recommended a number of precautions to obtain what he called "a normal boiling point", including the introduction of platinum wire to reduce bumping by acting as a source of air bubbles in the boiling liquid.[658] Even so, he concluded, "the

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[653] Kopp 1845, 167.
[654] Ibid., 169. Italics in original.
[655] Ibid., 169-170.
[656] Ibid., 171. Italics in original.
[657] Ibid., 172.
[658] Ibid., 173.

means of determining the boiling point accurately and with certainty must still be investigated".[659]

Although criticism of his proposal continued to accumulate over the following decade, Kopp remained adamant in its defence. In 1860, for example, his close friend Hofmann presented Kopp's summary of the evidence in support of a "law-like relation between the chemical composition of substances and one of their most important physical properties" to the Royal Society.[660] Kopp made no reference to the experimental method of boiling point determination in this paper, in which he used values published by a large number of chemists for a wide range of substances. Although Kopp generally took the values obtained by other chemists at face value, he indicated that certain results were more reliable than others. In some instances this was based on Kopp's opinion of the chemist at work. For example, measurements of the difference of the boiling points in one series of hydrocarbons by Arthur Church, one of Hofmann's assistants at the RCC, were singled out for particular praise.[661] Elsewhere, Kopp reminded his readers that "observations of boiling-points comprised in the higher ranges of the thermometer are frequently less accurate", whilst the boiling points reported for "the ethers of monobromoacetic acid, and especially those possessing higher boiling-points" were "not ... entirely to be relied upon" since these substances were "partially decomposed by ebullition".[662]

Kopp also identified several series of compounds whose boiling points "almost coincide, a circumstance which furnishes a valuable means of controlling boiling-point observations".[663] Problems of thermometry and questions of reliable technique may have been largely implicit in this paper, but there can be no doubt that Kopp was still pre-occupied with methods by which truly comparable data might be obtained. Where a simple law could be found relating boiling point and composition – as for the class of monobasic alcohols – "the determination of the boiling-point furnishes most material assistance in fixing the true character and position of a compound", and Kopp hoped that "the verification of the boiling-points of terms [members of a class] already known, and the examination of new terms" would lead to the discovery of other similar relations.[664] Once the boiling points of

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[659] Ibid., 174.
[660] Kopp 1860. This paper was read by Hofmann to the Royal Society on May 3, 1860.
[661] Ibid., 258, and fn referring to "A. Church (Phil. Mag. [4] ix. 256)".
[662] Ibid., 262 and 264.
[663] Ibid., 265.
[664] Ibid., 276.

enough compounds had been reliably and comparably measured, Kopp anticipated that boiling point might be a powerful tool in fixing the identity of a substance.

Hofmann contributed the only explicit discussion of experimental procedure in this paper, which is useful because it indicates the extent to which Kopp's earlier experimental concerns had been addressed by chemists with a less particular interest in boiling points. In a footnote concerning trimethylamine, Hofmann explained that whereas the sample whose boiling point of "between 4° and 5°" was reported by Kopp "had been prepared from the brine of salted herrings", he had recently "had an opportunity of determining the boiling-point of perfectly pure trimethylamine, prepared by the action of potassa on iodide of tetramethylammonium". Hofmann gave the boiling point as 9.3°, but this value had not been simply obtained. As he explained:

> *The ebullition of trimethylamine exhibits the irregularity so frequently observed in methyl-compounds. When the liquid ceases to boil freely, the thermometer is observed to indicate as much as 14° and even 15°, but the mercury falls again suddenly to 9°.3, when ebullition recommences.*[665]

Hofmann understood the need to use a "perfectly pure" sample and he took account of the problem of boiling point elevation during "abnormal boiling", but there is nothing in his brief report to indicate that particular care had been taken in the choice and preparation of the vessel used for the measurement.

Hofmann continued to take an active interest in boiling point measurements until the very end of his career. In 1889 he presented the results of a fresh investigation of the boiling points of the volatile aliphatic amines, including trimethylamine. According to Hofmann, Kopp's work had been influential in raising awareness of boiling point measurements with the result that "[e]veryone who found a new body felt the necessity of ascertaining its boiling point with care in the interest of the pursuit of these investigations". Not all of the boiling points measured previously were reliable, however, and Hofmann now claimed that "some doubts always remained, particularly with regard to the methyl compounds", where the small samples had perhaps not been absolutely pure.[666] Now, in 1889, Hofmann took advantage of temperatures around 10° below zero to subject these low-boiling compounds, which were now produced in large quantities in chemical factories, to a fresh investigation. The measurements were carried out in the laboratory of Adolph Bannow using apparatus recommended by the *Commission for the Development of*

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[665] Ibid., 274, and fn. added by "A.W.H.". Hofmann was criticising the boiling point determination carried out by his own student, Henry Winkles. See Hofmann 1889, 703.
[666] Hofmann 1889, 699.

*the Analytical Method of Fractional Distillation.*[667] Hofmann described the apparatus in some detail and also explained that the thermometer used, a Geissler thermometer, had been tested against a normal thermometer of the physikalischen [technischen] Reichsanstalt (PTR).[668]

The boiling point of trimethylamine determined in Bannow's laboratory at a pressure of 764.6 (mm mercury) and an air temperature of -5.2° was 3.2-3.8°.[669] This result showed "that the original determination of the boiling point of trimethylamine was the correct one and that trimethylamine therefore really boils at a lower temperature than dimethylamine [rather than at the higher temperature predicted by Kopp's rule for a substance of higher molecular weight]". Hofmann explained that the error in the later determination was partly due to the small sample size and partly the result of not having paid due attention to the air temperature. These comments on the sample size are particularly interesting: both the original 10 g of trimethylamine, and the 100 cubic cm later used in Bannow's laboratory involved extraordinarily large samples when seen from the perspective of synthesis.[670]

Despite the introduction of Regnault's method for determining boiling points during the 1840s,[671] the problem of measuring the boiling point of small quantities of substance accurately and reliably persisted into the 1870s and 1880s. In one approach to this problem the chemist Henry Chapman Jones, then a demonstrator at the Royal College of Science in London, developed what he called a "tension-tube", a modified U-tube fashioned from "a piece of ordinary quill tubing".[672] Describing the creation, preparation and use of the tension-tube took more than four pages of close typescript, at the end of which Jones explained the "exact corrections" needed to reduce the results obtained to standard conditions. Almost a page later he concluded, perhaps in somewhat weary triumph: "A temperature so obtained is designated simply the *boiling point.*" Jones reported that his method had been tested (once) by his Professor Edward Frankland, but it seems unlikely that such a cumbersome procedure was ever widely adopted. Jones himself desired only to "show the applicability of the process to the ordinary requirements of a

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[667] Ibid., 700. Bannow, then the director of C. A. F. Kahlbaum's chemical factory, had been the reporter for the Commission, set up by the Society for the Support of the Interests of the German Chemical Industry.
[668] Ibid., 700-701.
[669] Hofmann 1889, 703.
[670] Kopp 1860, 274; Hofmann 1889, 701.
[671] Silliman (1859, 308) described Regnault's method for measuring boiling point. See also Chang (2004, 74-84) for a discussion of Regnault's work on thermometry – and particularly the comparability of thermometers – during the 1840s.
[672] Jones 1878, 175.

laboratory, where the observation of boiling points is but of rare occurrence".[673] Despite this, Jones' report remains of interest because it illustrates the need to explain in detail *how* the boiling point was to be measured using a new piece of apparatus: in Jones' apparatus the boiling point was the "temperature at which the mercury is at the same level in both limbs" of the tension-tube.[674] Jones also paid careful attention to issues of standardisation, specifying not only the make of thermometer used (Negretti and Zambra), but also its calibration against "a Kew standard".[675]

Almost a decade later A. Siwoloboff published a new and ingenious solution to the problem of boiling point measurement which, unlike Chapman Jones' method, became a standard technique in chemistry and remained in general use until well into the twentieth century. Siwoloboff's method offered two main advantages over chemists' reliance on distillation as a means of measuring boiling point. First, it enabled the use of very much smaller samples, which was particularly helpful where only very small amounts of substance had been produced by synthesis. Second, it provided far greater standardisation of the measurement. Siwoloboff used a broken capillary tube to introduce a small bubble of air into the liquid whose boiling point was being measured. When a complete thread of small vapour bubbles was observed, Siwoloboff explained, "This is the moment when the thermometer indicates exactly the boiling point of the liquid under investigation".[676] The whole operation required the simplest possible apparatus, the most complicated element of which was undoubtedly the thermometer used for measuring the boiling temperature.

The examples I have used in this section show that chemists often specified the type and even the maker of the thermometer used in their experiments. As early as the 1830s, Liebig recommended that Wöhler use only thermometers made by the Parisian instrument maker Collardeau when performing organic analysis (discussed above). Well before the emergence of national standards laboratories such as the PTR, chemists in both England and Germany developed and recorded a marked preference for using thermometers manufactured by Heinrich Geissler of Bonn (Figure 16).[677] Geissler is now almost exclusively remembered for his creation of

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[673] Ibid., 180. Jones' comment indicates that organic synthesis, where such measurements were increasingly common, was not extensively practised at the Royal College of Science.
[674] Ibid., 178.
[675] Ibid., 180.
[676] Siwoloboff 1886.
[677] There are numerous references to Geissler thermometers in the chemical literature of both countries throughout the late-nineteenth century. In addition to Hofmann (1889) see,

Geissler tubes, elaborate glass vacuum tubes essential to the development of high vacuum physics during the later part of the nineteenth century, but I argue that his contributions to chemical science were far more significant.[678] I claim that specialist glassblowers, many of whom like Geissler founded firms for the large scale production of chemical glassware, played an essential role in solving problems of standardisation and supply. By transforming chemists' bespoke glassware solutions into widely available, standard commodity items, they both supported innovation in glass in chemical research and made it possible to equip Germany's rapidly increasing number of chemists in training with basic apparatus at reasonable cost.

When Geissler, who had served for many years as the *Mechanikus* of the University of Bonn, died suddenly in January 1879, this event prompted Hofmann to deliver a remarkable eulogy to the German Chemical Society in Berlin. Hofmann lavished praise on "this admirable, undemanding man", who "had developed the art of shaping glass before the lamp to a perfection, which none of his predecessors had achieved, and in which he, although he had trained excellent pupils, was unlikely to be soon surpassed".[679] Geissler combined an "absolutely astonishing" technical skill with "profound physical understanding", and it was this *combination* of abilities which enabled him to realise the ideas of chemists and physicists. Geissler contributed so much to the design of apparatus, Hofmann declared, that those who had commissioned them were not infrequently barely able to recognise their own thoughts in the items he produced.

Hofmann was evidently full of admiration for Geissler's success in transforming himself from a "simple glassblower" into the uncontested master of his art, but I want to draw particular attention to what Hofmann said about the means by which that transformation had been achieved. Denied the opportunity for continuous

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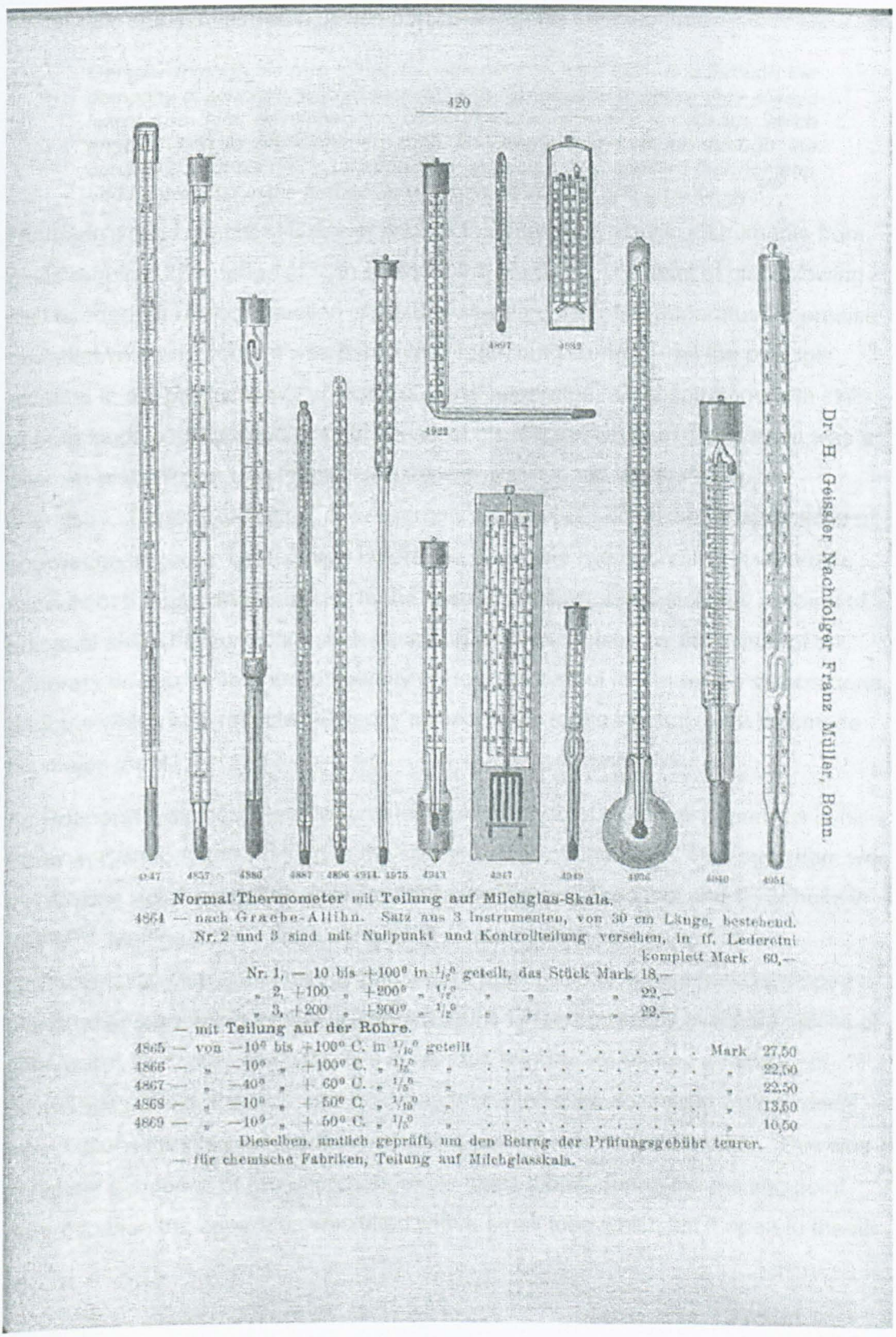
for example, Kopp (1866, 175) referring to "thermometers by Geissler of Bonn" obtained from Heinrich Buff in Giessen.

[678] See L'Estrange Turner (1992, 195) on Geissler tubes. Geissler has been sadly neglected by historians of chemistry, though his work on discharge phenomena with the physicist Julius Plücker during the 1850s has been discussed by the historian of physics Falk Müller (2004). See also Eichhorn (1984 and 1990); Kangro (1973); Feddersen and Oettingen (1898, 503-504).

[679] Hofmann 1879b.



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Dr. H. Geissler Nachfolger Franz Müller, Bonn.

4947 4857 4886 4887 4896 4911 4975 4943 4947 4949 4956 4960 4954

**Normal-Thermometer mit Teilung auf Milchglas-Skala.**

4864 — nach Graebe-Allihn. Satz aus 3 Instrumenten, von 30 cm Länge, bestehend. Nr. 2 und 3 sind mit Nullpunkt und Kontrollteilung versehen, in ff. Lederetui komplett Mark 60,—

Nr. 1, — 10 bis +100° in $^1/_2{}^0$ geteilt, das Stück Mark 18,—
„ 2, +100 „ +200° „ $^1/_5{}^0$ „ „ „ „ 22,—
„ 3, +200 „ +300° „ $^1/_2{}^0$ „ „ „ „ 22,—

— **mit Teilung auf der Röhre.**

4865 — von −10° bis +100° C. in $^1/_{10}{}^0$ geteilt . . . . . Mark 27,50
4866 — „ −10° „ +100° C. „ $^1/_5{}^0$ „ . . . . . „ 22,50
4867 — „ −10° „ + 60° C. „ $^1/_5{}^0$ „ . . . . . „ 22,50
4868 — „ −10° „ + 50° C. „ $^1/_{10}{}^0$ „ . . . . . „ 13,50
4869 — „ −10° „ + 50° C. „ $^1/_5{}^0$ „ . . . . . „ 10,50

Dieselben, amtlich geprüft, um den Betrag der Prüfungsgebühr teurer.

— für chemische Fabriken, Teilung auf Milchglasskala.

Figure 16. This page from his 1904 catalogue shows some of the large range of thermometers available from Geissler's successor Franz Müller.

systematic study in his youth, it was particularly in his later life that:

> *Geissler through his rare talent, through his iron hard work and through the company of scholars, who associated with him eagerly because they always learnt from him, developed the comprehensive scientific knowledge which enabled him to participate in such an outstanding manner through the construction of his precision apparatus, especially his standard thermometer and hydrometer in the further development of science and technology.*[680]

Hofmann's assessment of Geissler implies that making scientific instruments from glass required knowledge of both science *and* glass.[681] The level of glassblowing skill needed for the construction of reliable standard scientific apparatus for precise quantitative measurement was particularly high, but I contend that the principle extends to the production of all kinds of glass apparatus. Only someone with skills of both kinds could produce useful chemical glassware, whether that person was a chemist-glassblower or a master glassblower with a good understanding of chemistry. For any individual, it was largely a matter of circumstance which kind of knowledge began to be acquired before the other, the two becoming inseparable aspects of thought and practice. In the case of Geissler, his matchless melding of artisanal skill with intellectual understanding was recognised by the award of an honorary doctorate from the University of Bonn as part of its centenary celebrations, a tribute which also reflected Geissler's importance to the institution he had made his major client.[682]

As Hofmann indicated, Geissler created a wide range of chemical apparatus in his Bonn workshop, often working to the specifications of chemists. One such item was the melting point apparatus Geissler made for Richard Anschütz and G. Schultz in 1877.[683] Melting point – like boiling point – was by then recognised as a characteristic value and a useful measure of purity, and chemists had developed a standard approach to its measurement (Figure 17) using readily available pieces of glassware. Anschütz and Schultz's apparatus (Figure 18) offered a number of advantages. First, the sulphuric acid was protected from absorbing water, which would dilute it and so reduce its own boiling point closer to that of water. This was achieved by means of two interchangeable glass tubes: during the melting point determination the apparatus was fitted with a small tube which left it open to the air

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[680] Hofmann 1879b, 148.
[681] Körner (1831, 4) expressed a very similar opinion, singling out the glassblower Michael Greiner for particular praise.
[682] Hofmann 1879b, 148.
[683] Anschütz and Schultz 1877. Anschütz was called to the chair in Bonn in Hofmann's stead in 1865.

which separates from the filtrate on cooling is filtered off at the pump, and dried in a vacuum desiccator. If it be not white in colour, the crystallisation from hot water with addition of animal charcoal must be repeated. The purity of the product is controlled by the determination of its melting point. For this purpose a small quantity of it is dried, powdered, and introduced into a capillary tube (fig. 4). The determination is carried out in the apparatus shown in fig. 5. The flask is about four-fifths filled with concentrated sulphuric acid. The thermometer reaches to the middle of the liquid and is supported in a cork which is placed loosely in the neck of the flask. The capillary is stuck to the thermometer, which is wetted with a little sulphuric acid, in such a position that the substance is at the centre of the

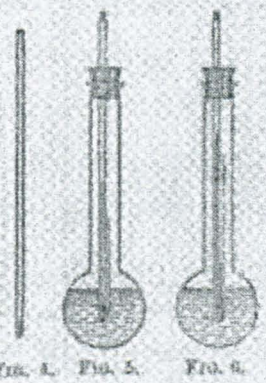
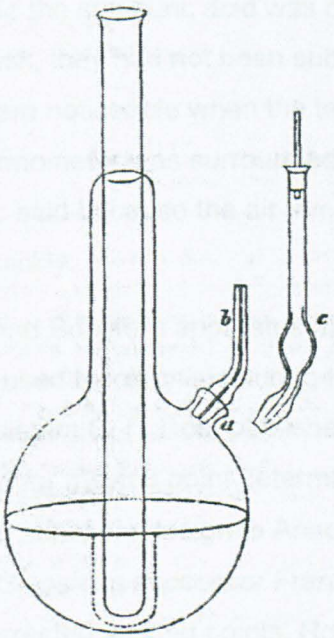


FIG. 4. FIG. 5. FIG. 6.

Figure 17. Fischer (1909, 10) illustrated a standard melting point apparatus. The sample was contained in a glass capillary tube placed, with the thermometer, inside a round-bottomed flask filled with concentrated sulphuric acid of paraffin. The liquid in the flask was quickly and evenly heated, either by stirring or by moving the flame in circles beneath it. See also Anschütz and Schultz (1877) and Baeyer (1886).

belästigt. Man kann in dem beschriebenen Apparat unter Anwendung von Schwefelsäure Schmelzpunkte wie den des Antrachinons mit Leichtigkeit nehmen, ohne etwas vom Schwefelsäuredampf auch nur zu merken, da sich alle Dämpfe im oberen Theil des Apparates condensiren. Der Apparat ist immer zur Verwendung fertig und bedarf keiner beständigen Aufsicht, da in ihm die Temperatur nur langsam steigen darf, wenn man genaue Resultate bekommen will. Letzteres gilt besonders für die Schmelzpunkte niedrig schmelzender Verbindungen. In der beifolgenden Tabelle sind einige Schmelzpunktbestimmungen gegeben. Bei Apparat I befand sich etwas Asbest unten im Reagenscylinder, und der Kolben war rund, bei Apparat II befand sich kein Asbest im Reagenscylinder, und der Boden war eingedrückt.




Bei einem Barometerstand von 759 Mm. zeigte das im Apparat I verwandte Thermometer:

im Wasserdampf 100.5°
im Naphtalindampf 217.5°;

das im Apparat II verwandte Thermometer:

im Wasserdampf 100°
im Naphtalindampf 216.5°.

Figure 18. This modified melting point apparatus, made for Anchütz and Schultz (1877, 1801) by the Bonn glassblower Heinrich Geissler, addressed three practical problems with the existing method of melting point determination. It helped to maintain the thermometer at a more even temperature by encasing it in an air bath within the sulphuric acid bath. It also protected the sulphuric acid from degradation, mainly because the apparatus was partially closed and protected by a drying tube when not in use. The chemist, moreover, was no longer exposed to unpleasant and corrosive acid fumes when carrying out the measurement.

to allow for expansion. This tube was replaced by a calcium chloride drying tube when the apparatus was being left to cool. In this way, Anschütz and Schultz claimed, they had been able to use the same sulphuric acid for over half-a-year. Second, because the sulphuric acid was contained inside a covered vessel, rather than an open flask, they had not been subjected to the "damaging and unpleasant fumes" which were noticeable when the temperature exceeded 200°. Finally, the fact that the thermometer was surrounded by air and not fluid removed the need to stir the sulphuric acid because the air temperature around the thermometer evened out extremely quickly.

Both Anschütz and Schultz's apparatus and the earlier, open-flask method continued to be used by chemists during the following decade but in 1886 Ladenburg's assistant C. F. Roth published a paper in which he proposed a new, standard method for melting point determination.[684] Roth's apparatus (Figure 19), which was rather similar in design to Anschütz and Schultz's, had been made for him in Bonn by Geissler's successor Franz Müller.[685] In addition to the difficulty of comparing uncorrected melting points, Roth explained that melting points determined by the two current methods in general use gave different results, Anschütz and Schultz's method tending to give higher readings. Roth explained why the incomparability of the results obtained in different ways reduced the value of melting points in chemistry:

> *For some who determine the melting point of a new body, its plain melting might be the main goal of the operation. For another, however, who wishes to use the melting point later as an aid to the identification of compounds, a perfect agreement of his found melting point with that previously stated is most highly desired, indeed necessary for him.*[686]

Roth compared the melting points of six substances determined using the new apparatus, which he had been using for at least a year, with those obtained using "free sulphuric acid". He was careful to explain that he had used "one and the same thermometer" for both sets of measurements, even going so far as to specify the extent of submersion of the thermometer in the acid in the two different pieces of apparatus. In addition to benzoic acid and urea, two relatively well-known, simple organic substances, Roth included the melting points of the mercury double salts of α-picolin and pyridine.[687] Chemists frequently made salts since they could usually

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[684] Roth 1886.
[685] Ibid., 1973, gave the provenance of his apparatus. Roth (and Ladenburg) were then working in Kiel. Müller was described as "Geissler's successor" by Schiff (1885, 1540).
[686] Roth 1886, 1970-1971.
[687] Ibid., 1972.

In einen Rundkolben *a* von 65 mm Durchmesser und 200 mm langem, 28 mm weitem Halse *b* ist ein 15 mm weites Glasrohr *c* bis 17 mm vom Boden des Rundkolbens eingelassen. Dieses Rohr ist unten geschlossen, oben bei *g* mit dem Kolbenhalse *b* verschmolzen. Bei *d* ist ein 11 mm weiter Tubus eingelassen, welcher seitlich eine runde Oeffnung besitzt. In diesen Tubus passt ein eingeschliffener, hohler Glasstöpsel *e*, an welchem sich gleichfalls eine seitliche Oeffnung befindet.

Vor dem Gebrauche wird der Kolben *a* durch den Tubus mit concentrirter farbloser Schwefelsäure bis zur Marke *f* etwa gefüllt, dann wird der Stopfen *e* so eingefügt, dass die beiden seitlichen Oeffnungen von *e* und *d* correspondiren. Wird nun die Schwefelsäure erhitzt, so steigt sie in *b* in die Höhe und so befindet sich ein in *c* eingeführtes Thermometer bis nahezu 280° in einem von heisser Schwefelsäure umschlossenen Luftbade.

Meine nächste Aufgabe bestand darin, nachzuweisen, ob in diesem Luftbade überall eine gleiche Temperatur herrsche oder ob in verschiedener Höhe desselben Temperaturdifferenzen auftreten. Letzteres ist der Fall; doch sind die gefundenen Differenzen sehr geringe. Beim Anwärmen (60 bis 70°) besteht eine Differenz von 8°, die sich

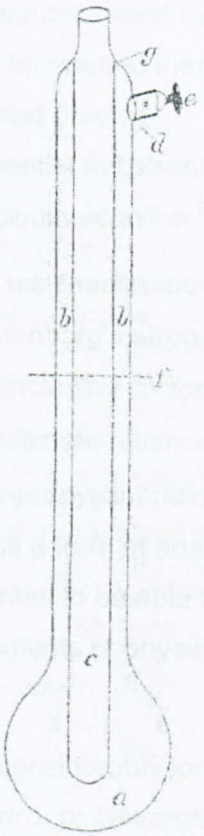


Figure 19. The main difference between Roth's (1886, 1971) apparatus and its predecessors is its much more elongated neck, which became partially filled with sulphuric acid during use. This minimised the variation of temperature with height inside the air bath surrounding the thermometer, and hence the need to correct the recorded boiling point. According to Roth's trials – which included measuring the melting point of the mercury double salt of α-picoline, the starting material for Ladenburg's synthesis of coniine – the largest correction that would ever be necessary was 0.16° C, a figure well within the accuracy of the available methods of correction.

be highly purified by crystallisation, and their purity then demonstrated by quantitative analysis. As I explain below, Ladenburg had introduced mercury double salts for exactly this reason, the preparation, purification and precise characterisation of both pyridine and α-picoline being essential to Ladenburg's successful syntheses of pyridine and piperidine bases including coniine.[688]

Roth's work on the standardisation of melting points, and his development of a new apparatus for measuring them, coincided exactly with Ladenburg's struggle to determine whether any of his candidate synthetic bases (including *α-isopropyl-* and *α-propylpiperidine*) was identical to coniine, and with his ultimate reliance on melting point to establish the identity of synthetic *dextrorotatory α-propylpiperidine* with natural coniine. Where synthesis was being carried out as a form of analysis, in order to establish the identity of a substance, it was essential to be able to produce reliable, accurate and – above all – *comparable* measurements of physical properties.

Chemists might have been measuring melting points for considerably longer than they had been determining whether a substance was *dextro-* or *laevorotatory* but, as this section has shown, producing adequately standardised values for melting and boiling points was no easy matter. Envisaging and fashioning functional glassware, making it reliably replicable in both form and function, and producing it on a large scale drew on the combined intellectual and artisanal skills of chemists and glassblowers. Furthermore, the division of labour involved in transforming innovative thinking into standardised material objects did not follow the traditional view of scientist-technician relations.[689] Constructing the new criteria of chemical identity relied on two complementary aspects of working in glass: flexibility and standardisation. Glass offered huge potential for adapting existing apparatus but, in the hands of skilled specialists like Geissler, a piece of glassware could also be transformed into a highly standardised item incorporating localised expertise within a material object which could – once carefully packed - be made to travel. Working in glass made it possible to manage chemical processes in previously unimagined ways, partly through standardisation of apparatus and technique but also because the chemist simultaneously retained creative control over his world-within-glass.

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[688] Ladenburg (1888, 4-7) presented the analyses and melting point data of pyridine and α-picoline in this synthetic context.
[689] Jackson (2008) discussed this issue in the context of Liebig's Giessen laboratory.

## The Synthesis of Coniine and the Origins of the Synthetic Organic Chemist

> *It has been found in many cases that the earlier analytical method is not sufficient for establishing the chemical nature of a compound, and that the synthetical method constitutes a necessary complement. The first method usually precedes the second; but, in the history of a substance, its synthesis, with rare exceptions, marks a period, and, with it, the interest which the scientific investigation of the substance presents is usually at an end.*
>
> *Albert Ladenburg (1900)*[690]

By the 1880s many chemists were engaged in the constitutional analysis and attempted synthesis of the natural alkaloids. In concluding my case study of coniine I explain how Ladenburg, whose alkaloid research had previously focused on the belladonna alkaloid atropine, became interested in the synthesis of coniine. I argued in the previous chapter that Hofmann viewed the synthesis of coniine in largely conceptual terms. Here, by contrast, I contend that Ladenburg's emphasis on producing coniine by means of synthesis was a significant motive for his efforts to bridge the gulf between conceptual and actual synthesis, and that it was powerful in enabling his success – partly because this constructive focus caused Ladenburg to direct his research towards extremely specific goals. Determining the absolute constitution of coniine and classifying its related compounds were relevant to Hofmann's broader research programme, for example, but Ladenburg wasted no effort investigating anything not directly relevant to the synthesis of coniine.

I begin by using Ladenburg's published papers to show that, despite this fixity of purpose, his route to the synthesis of coniine was by no means straightforward. Synthesising coniine involved Ladenburg in preparing numerous isomeric substances, which he struggled to differentiate and identify. Only by demonstrating that one of his synthetic products (*dextrorotatory α-propylpiperidine*) was identical with natural coniine was Ladenburg able to settle the final details of coniine's constitution and claim its synthesis. According to Ladenburg's papers, achieving the synthesis of coniine required a lot more than the ability to effect a particular chemical transformation, difficult though that was.

I then illustrate how Ladenburg's success depended critically on his development of new glassware-based techniques both for the purification of his starting materials and in order to solve some tricky problems of chemical identity. The different aims of Ladenburg's target-oriented approach to synthesis meant that he was confronted by new challenges, in response to which he developed both new reactions and a

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[690] Ladenburg 1900, 288-289.

body of novel skills and experimental techniques, all of which clearly differentiate his chemical practice from Hofmann's. In particular, I show that many of the components of this new practice relied on innovative, glassware based approaches to the reaction, purification, characterisation and identification of organic compounds, and I therefore argue that this emergent practice of synthetic organic chemistry depended crucially on the development of chemical glassware and the appropriation of glassblowing skills by chemists.

During the period between 1879 and 1883, Ladenburg's alkaloid research focused on the constitution and synthesis of tropine, the nitrogenous base found in atropine.[691] This topic was attractive to Ladenburg because: "The problem of the synthesis of alkaloids has still not been solved in a single case, and it is therefore already of importance, when even a step in this direction succeeds".[692] Ladenburg undertook a series of "investigations of a synthetic nature" but, although he was able to produce some interesting homologues of natural atropine, the synthesis of tropine and hence the elucidation of its constitution proved difficult.[693] In 1881 Ladenburg, who was keen "to keep the undisturbed continuation of [this research] to himself", published a detailed account of his attempts to synthesise tropine.[694]

Two years later, Ladenburg was able to publish a more comprehensive study of the constitution of atropine in which he proposed that tropine was related to pyridine and piperidine, just as Hofmann had shown coniine to be.[695] Tropine and coniine were therefore constitutionally related, both belonging to what Ladenburg later termed the "pyridine series" of alkaloids.[696] In 1884, Ladenburg published the preparation of γ-ethylpiperidine by reduction of its pyridine analogue, a discovery which aroused the "hope of thereby making possible the synthesis of coniine".[697] Ladenburg immediately pursued this enticing possibility, reporting his syntheses of a range of possible candidate compounds.

The first two compounds he made turned out not to be coniine, but Ladenburg showed that they were closely related compounds in which the propyl group

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[691] Ladenburg's research interests ranged widely, including analytical and synthetic methods, investigations of organozinc, -tin, and –silicon compounds, and his well known proposal of a prismatic constitution for benzene. Ladenburg's alkaloid research was restricted to atropine and related compounds.
[692] Ladenburg 1879, 941.
[693] Ladenburg 1881a.
[694] Ladenburg 1881b, 235 (negative results not included), 233 (direct quotation).
[695] Ladenburg 1883b, 149. Many of the methods Ladenburg used here were those developed by Hofmann for the constitutional analysis of coniine.
[696] Ladenburg 1888b, 1-98.
[697] Ladenburg 1884a, 391.

occupied a different position on the piperidine ring (*β- and γ-propylpiperidine*).[698] Soon after this he published the synthesis of *α-isopropylpyridine*, which he expected to be able to reduce to coniine. When Ladenburg performed this reaction, the product again turned out not to be coniine. Ladenburg had confirmed that the propyl group in coniine was attached to the carbon next to nitrogen (the α position) but he remained in doubt as to whether it was branched (*α-isopropylpiperidine*) or not (*α-propylpiperidine*).[699] He had initially made rapid progress towards the synthesis of coniine but only the production by synthesis of a compound identical to coniine would enable Ladenburg to resolve this final constitutional question, which Hofmann's work had left unsolved.

Anticipating that coniine's propyl side chain would be branched, Ladenburg set out with the goal of "proving the identity of α-isopropylpiperidine with coniine". When he prepared this compound and compared its properties with carefully purified natural coniine, however, he found that the two were not the same. Ladenburg did not immediately conclude that coniine must contain a straight chain propyl group. Rather as Schiff had done some fifteen years earlier, Ladenburg preferred to attribute the small differences in properties to the presence of isomeric substances in his synthetic product. "It is possible", he proposed, "that if one were to succeed in separating the base into its two active components, the dextrorotatory part will prove completely identical to coniine".[700] It took Ladenburg a lot more work, including the preparation of synthetic conyrine (*α-propylpyridine*), to satisfy himself that coniine was *α-propylpiperidine*.[701]

When Ladenburg at last focused his attention on the synthesis of *α-propylpiperidine*, we might expect him soon to have been successful. Yet despite his vast accumulated experience in the preparation of substituted pyridines, Ladenburg's early attempts failed. Even when, in 1886, Ladenburg was able to report "the synthesis of a base extremely similar to coniine", he claimed only that this was very probably "chemically identical" to coniine.[702] Ladenburg's caution reflects the fact that, although the standards of evidence required to demonstrate chemical identity were much clearer than they had been fifteen years earlier, obtaining such evidence was by no means easy. Just as with his earlier work on tropine, Ladenburg was

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[698] Ladenburg 1884c, 774-775.
[699] Ladenburg and Schrader 1884, 1123.
[700] Ladenburg 1884b, 1676. (Received 18 July 1884.)
[701] Ladenburg 1885, 1589. (Received 12 June 1885.)
[702] Ladenburg 1886b, 439-441.

eager to publish in order to establish his position in a competitive field, but he wisely admitted that the identity of his synthetic base to coniine was not yet proved. Ladenburg repeated his synthesis "with chemically pure material and in larger scale" in order to settle the question. Later that year his *Synthesis of Active Coniine* demonstrated that his synthetic product was identical to natural coniine by minutely comparing their chemical and physical properties.[703] Ladenburg's cautious approach was rewarded when – in sharp contrast to Schiff's experience – his synthesis was rapidly recognised as successful.[704]

Just as with Hofmann, Ladenburg's behaviour must also be seen within the context of his research as a whole. From the outset, Ladenburg had concentrated his alkaloid research on a highly restricted area, namely the study of atropine, the synthesis of tropine, and a few other very closely related problems.[705] During that research, Ladenburg developed a number of reactions which were useful in making synthetic pyridine and piperidine bases, as a result of which he extended his interests to include the piperidine base coniine.[706] For Ladenburg, I contend, coniine was nothing more than a suitable target for transformational knowledge gained elsewhere. Unlike Hofmann, for whom constitutional investigations of coniine and its related compounds were a powerful means to developing understanding of entire classes of nitrogenous compounds, Ladenburg's interest in coniine was highly focused on its synthesis and he regarded its constitution in largely operational terms as a result.

Ladenburg was considerably occupied by the question of whether coniine was *α-propyl* or *α-isopropylpiperidine* because this affected his ability to achieve the synthesis of coniine. On the other hand, he did *not* adopt Hofmann's graphical representation of piperidine and pyridine, coniine and conyrine as nitrogen-containing carbon rings, this constitutional representation of pyridine being directly analogous to that proposed for benzene by Kekulé in the mid-1860s.[707] Although he had trained with Kekulé in Ghent and worked on benzene derivatives during 1865,

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[703] Ladenburg 1886a, 2578-2583.
[704] Ibid., 2583. Ladenburg's work was well received by the 1886 German *Naturforscherversammlung* in Berlin.
[705] Ladenburg 1879.
[706] Ladenburg 1886a, 439; and on synthetic methods, Ladenburg 1883a.
[707] Ladenburg (1888b, 50 and 54-55) presented experimental evidence for the ring constitution of pyridine and piperidine, which he represented "according to the Körner-Dewar hypothesis".

Ladenburg remained unconvinced by Kekule's theory until at least 1890.[708] He fiercely disputed the benzene theory elsewhere, but made no comment in any of his work on coniine regarding the constitutions of piperidine and pyridine. It seems that – contrary to Graebe's view – aromatic structure theory was of little relevance to Ladenburg's synthesis of coniine. What *was* important was that he could produce the desired end product by means of suitable chemical transformations.

I mentioned in Chapter Three that one of these transformations, by means of which Ladenburg had succeeded in preparing various substituted pyridines, was similar to an earlier reaction developed by Hofmann for the production of substituted anilines. The disagreement between the two chemists about the apportioning of credit for the new reaction prompted Ladenburg to defend the originality and significance of his own contribution. His forceful rebuttal of Hofmann's claim appeared in 1888, at the start of a detailed summary of his work on pyridine and piperidine bases including coniine. This paper is worth examining because it demonstrates that the questions and difficulties confronting Ladenburg were very different from those preoccupying Hofmann, and because it describes the solutions Ladenburg found in considerable practical detail.[709]

Although when he first reported the preparation of ethylpyridine in 1883, Ladenburg had described the new process as "the application of a reaction which led A. W. Hofmann to the preparation of the homologues of aniline",[710] in 1888 he emphasised that making the new reaction work had not been easy: "Even I worked for a long time in vain, until I found the method".[711] Ladenburg may initially have been pleased to connect his reaction with one discovered by the famous Hofmann but five years later he was conscious of just how much work had been involved in converting a conceptually plausible transformation into a synthetically viable chemical reaction.[712] It might be sufficient in Hofmann's world to infer the possibility of a particular reaction from reasonable constitutional analogy; in Ladenburg's nothing less than the reliable ability to effect the desired transformation in adequate yield, and without undue risk, would do.

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[708] Rocke (1985, 375) noted that Ladenburg's demonstration of the chemical equivalence of all six carbon atoms in benzene provided essential support for Kekulé's constitution as well as his own, but Ladenburg continued to defend his own prism constitution for benzene until around 1890. See Ladenburg 1869a, 140-142, and *idem.* (1872) for the original exposition of Ladenburg's ideas. Ladenburg (1887 and 1890) make clear that he did not accept Kekulé's ring formula for benzene until at least the 1890s.
[709] Ladenburg 1888b.
[710] Ladenburg 1883a, 1410.
[711] Ladenburg 1888b, 2.
[712] On the development of this reaction, see Ladenburg 1883c and 1884c.

Ladenburg's eventual route to coniine involved the reduction of α-allylpyridine prepared from α-picoline. Although the status of this synthesis as total depended on the fact that α-picoline could, in principle, be prepared from its constituent elements, in practice Ladenburg and his assistant Dr. Lange had obtained it from commercial picoline (derived from coal tar) by distillation. Ladenburg explained in 1888 that: "This base can *now* be separated from commercial picoline with great ease and security", and he continued to describe the procedure:

> *50 g of the fraction 128 to 134° obtained [from commercial picoline] by distillation were dissolved in 170 g diluted, approximately 11 percent hydrochloric acid, a little fuming hydrochloric acid added and then mixed with a hot solution of 312 g mercuric chloride in 4500 g water. On cooling the double salt crystallised in large glittering prisms and leaves. Several hours later the pyridine double salt also begins to crystallise in the characteristic fine needles and this is the moment when the mother liquour must be separated by filtration.*[713]

Obtaining pure α-picoline, therefore, not only depended on fractional distillation but also on a process of fractional crystallisation which required the chemist to be able to distinguish between different crystal forms appearing within a single glass flask.[714]

Ladenburg's introduction of separation using mercuric chloride was not his only innovation in the purification of compounds related to pyridine. As he had explained in the introduction to this paper, obtaining pyridine bases in pure form had required "very careful and multiple repeated fractionations" using a special distillation flask which had been in use for many years in his laboratory. "These flasks", he explained, "whose extremely elongated neck is blown into many bulbs, ... have proved very practical, much better than the usual flasks with bulb-shaped attachments or similar." It was clearly important to Ladenburg that others should be able to obtain such flasks, for he not only mentioned in a footnote that they could be obtained "in various sizes" from the firm Desaga in Heidelberg, but included a diagram of such a flask with this paper, presumably with the thought that it would serve as a guide for glassblowing (see Figure 15, p.197).[715]

Ladenburg's description of his method for obtaining pure pyridine bases was, I suggest, not merely intended to be helpful to other chemists. It also represented a claim to superior technique and an advertisement of what was involved in doing chemistry this way. For example, Ladenburg deprecated the fact that textbooks

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[713] Ladenburg 1888b, 5-6. Emphasis added.
[714] Fractional crystallisation relies on differential solubility to achieve separation: less soluble compounds crystallise sooner than more soluble.
[715] Ibid., 3-4.

continued to report the properties of pyridine obtained on an impure sample, no chemist having taken on "the easily solved task" of separating pure pyridine. Ladenburg had "therefore undertaken this small effort, in order to determine the physical properties of this base". Pyridine purified by Ladenburg's method, which involved both the innovations described above, had a boiling point of 114° C which "remains constant to the last drops", an indicator of the highest possible purity and a benchmark against which the preparations of all future chemists could be measured.[716]

Ladenburg claimed that "α-picoline enters easily into reaction with aldehydes",[717] but his preparation of α-allylpyridine by this method was far from straightforward. Ladenburg obtained 262 g pure α-picoline from 600 g commercial picoline. When he heated this pure α-picoline with paraldehyde in ten sealed tubes only a small proportion was converted into α-allylpyridine, much of the α-picoline remaining unreacted. This unconverted starting material was recovered and twice reacted again with the aldehyde, but even so the final yield of crude product was around 36 g. Ladenburg succeeded in obtaining sufficient pure α-allylpiperidine for analysis, but he was forced to sacrifice 4 g of his product to oxidation by calcium permanganate in order to be sure that it was really the α-compound.[718]

Such low yields were by no means uncommon. Ladenburg's preparation of ethylpyridine, for example, produced 667 g raw product from 800 g pyridine by means of a reaction carried out in 267 sealed tubes! On purification, he obtained 105 g α-compound and 54 g γ-compound.[719] Such procedures were inevitably extremely labour intensive, so it is no surprise to find that Ladenburg was "essentially supported" by a dozen students and assistants whose long hours in the laboratory helped to establish what remains a distinctive feature of synthetic organic chemistry.[720] Another consequence of such poor yields was that the scale of each subsequent reaction in a multi-step synthesis diminished very rapidly. As the examples I have given show, chemists often had to begin with very large quantities of starting materials in order to obtain enough product for complete characterisation, but the later stages were often carried out on relatively small quantities. Chemists

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[716] Ibid., 4-5. The absence of a constant boiling point was recognised by this time as indicating a mixed substance. See, for example, p. 14 on the raw product of the preparation of α-ethylpyridine.
[717] Ibid., 8.
[718] Ibid., 26-28.
[719] Ibid., 15.
[720] Ibid., 4.

therefore became skilled in handling substances in widely varying amounts. Often this could be achieved by using essentially the same technique in different sized apparatus, as in the case of Ladenburg's distillation flask. Other techniques, meanwhile, were only applicable to a restricted range of sample size and in these cases, for example the use of sealed tubes, larger scale working was achieved by multiplying up the process.

Completing the synthesis of coniine, Ladenburg found that the reduction of α-allylpyridine by sodium in boiling alcohol "produces not only very good (almost theoretical) yield, but also directly an almost pure product".[721] The melting point of the synthetic base was 166 to 167°, compared with 166 to 166.5° for coniine, its analysis agreed with the formula $C_8H_{17}N$, and it showed "the greatest similarity with coniine and may be regarded as chemically identical to it".[722] Nevertheless, the chemical identity of the synthetic and natural bases was not finally proved for Ladenburg until he produced the aromatic base conyrine and its blue fluorescent by-product from them both.[723] Here, too, Ladenburg used a comparison of the melting points of the platinum salts of conyrine produced from both sources as a key piece of evidence for their identity.[724]

Ladenburg's synthesis of coniine tells us a lot about the nature of the constitutional knowledge required for synthesis in the nineteenth century. It shows that although some constitutional knowledge was necessary for synthesis, this did not necessarily include those aspects subsequently regarded as most important. Hofmann may have chosen to represent coniine and conyrine using graphical formulae reflecting aromatic structure theory but – despite Graebe's emphasis on the importance of the aromatic theory for the synthesis of alkaloids – Ladenburg did not adopt such formulae until several years after his synthesis of coniine. It is also worth noting how little of the work I have described here made any reference to the position of atoms in space. Although this concept had first been introduced more than ten years earlier, chemists continued to work principally with constitution rather than absolute three-dimensional structure. Constitutional knowledge, moreover,

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[721] Ibid., 80.
[722] Ibid., 81.
[723] Ibid., 82-83.
[724] Ladenburg 1886a, 2580. The melting point of the platinum salts were: 158-160° for conyrine produced from the synthetic base; 159-160° for that from natural coniine.

continued to be derived mainly from the study of chemical transformations, with the result that these remained the principal points of reference for that knowledge.[725]

Given that constitutional knowledge could only be gained from studying reactions, it was entirely reasonable to attempt synthesis based on provisional constitutional knowledge. In the case of coniine, it was possible for Ladenburg to suspend judgement concerning the constitution of the nitrogen-containing piperidine moiety of the molecule. Only following his synthesis of piperidine in 1888 did Ladenburg consider that its ring constitution was "finally established" and, convinced that "a ring formula is fitting for pyridine", Ladenburg used graphical formulae to represent piperidine and its related compounds as nitrogen-containing rings thereafter.[726]

Ladenburg's 1886 synthesis of coniine both depended on, and confirmed, its constitution, but in 1888 he gave a rather minimal account of the earlier constitutional investigation of coniine. Although he acknowledged Hofmann's role in revising the formula of coniine to $C_8H_{17}N$ and in the production of the pyridine base conyrine $C_8H_{11}N$, Ladenburg omitted to mention Hofmann's elucidation of the position of the propyl group and that it was Hofmann who had firmly established the constitutional relationship between piperidine and pyridine. Instead, Ladenburg chose to emphasise his separation of the dextrorotatory natural isomer of coniine from the optically inactive product of his original synthesis, the first such separation of its kind. Of course it is entirely understandable that Ladenburg would emphasise his own contribution, particularly since he felt this had been undervalued by Hofmann, but I propose that Ladenburg also wished to emphasise a new kind of chemical expertise.

Ladenburg's paper repeatedly referred to the extreme care devoted to obtaining pure substances, to the methods by which that purity had been verified, and to the precise operational details by which particular chemical reactions had been performed. He comprehensively reported the facts and figures by which the identity of his products was demonstrated. Many of Ladenburg's procedures relied on his use of glassware, both composite glass apparatus constructed from standard items and custom-blown pieces. He extolled the virtues of innovative glass apparatus developed to solve specific technical problems, but Ladenburg's practice also

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[725] See for example Sadtler 1883 on the current knowledge of the constitution of coniine and quinine in 1883/4. Samuel Sadtler was Professor of Chemistry at the renowned Philadelphia College of Pharmacy.

[726] Ladenburg 1888b, 52-55, and especially 54-55 on the constitution of piperidine and pyridine.

depended on the more traditional benefits of working in glass. For example, it was often crucial to the success of his syntheses that the chemist responded to visual indicators of chemical change at just the right moment, only glass apparatus giving the chemist access to such immediate visual feedback.

Ladenburg's attitude to synthesis, expressed in the epigraph to this section, certainly acknowledged its complementary role in relation to other established forms of analysis, but there can be no doubt about the dominance of constructive synthesis in his view of chemistry.[727] For Ladenburg, claiming "the first total synthesis of an alkaloid" was the ultimate goal, to which all other aspects of his chemistry were subservient.[728] Ladenburg's approach, aims and skills as I have described them differentiate him very clearly from chemists like Hofmann, for whom synthesis was a means to an end, merely one of a number of methods of expanding knowledge about the material world. In this respect, Ladenburg's synthesis of coniine has much in common with twentieth-century syntheses that celebrated the constructive power of organic chemistry, and because of this I believe it appropriate to describe Ladenburg as one of the first *synthetic organic chemists.*

## Conclusion

I have used my case study of coniine (Chapters Three and Four) to show that the practice of organic synthesis as a constructive art diverged from the performance of *synthetical experiments* aimed at the acquisition of primarily analytical knowledge during the late-nineteenth century. Comparing the breadth of Hofmann's research into a wide variety of natural and artificial nitrogenous bases with Ladenburg's much narrower focus on the artificial preparation of the natural alkaloid coniine illustrates the increasingly specialised experimental practice of a new generation of *synthetic organic chemists.* It also begins to explain why successful synthesis was such an immensely time-consuming and labour intensive process. In the case of coniine, Ladenburg made several compounds before he was able to demonstrate that one of them was identical to coniine, thereby finally establishing its constitution (and structure). Knowing that he wished to synthesise coniine did *not* mean that Ladenburg knew, in constitutional (or structural) terms, exactly what he wanted to make. Late-nineteenth century organic synthesis, far from being a straightforward

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[727] Ladenburg (1883b, 149) expressed exactly this attitude in relation to tropine: "Trotzdem halte ich meine Aufgabe noch nicht für gelöst. Es bleibt mir die Synthese des Tropins aus Pyridin oder Piperidin auszuführen, womit ich schon längere Zeit beschäftigt bin."
[728] Ladenburg 1888b, 83-86. Quotation from p. 86.

*consequence* of complete constitutional (or structural) knowledge, was an essential means of producing that knowledge.

This study also highlights the inadequacy of equating the practice of synthesis to the performance of chemical transformations. The synthesis of coniine certainly involved the development of reliably reproducible reactions by means of which highly specific, as opposed to generic, chemical transformations could be achieved. But it also depended critically on Ladenburg's ability to obtain both starting materials and products in previously unattained levels of purity, and to differentiate between numerous isomeric substances whose chemical properties were otherwise almost identical using minute differences in a growing range of physical properties. Merely doing reactions – as any modern synthetic organic chemist would confirm – was only part of a practice in which the skills of purification and characterisation were equally essential and at least as time-consuming.

Every aspect of the practice of synthesis, moreover, depended on a variety of novel uses of glass apparatus. Synthetic chemists like Ladenburg skilfully exploited the new possibilities chemical glassblowing offered for innovation and standardisation alongside glassware's more traditional benefits, such as transparency and chemical inertia. Many important aspects of this new glassware-based practice were peculiar to synthetic chemistry, being directly involved in processes of purification, transformation and identification. Others, such as the development of comparable thermometry and characteristic melting and boiling points, spanned the boundary between chemistry and physics. In either case synthetic organic chemists mobilised the experimental possibilities of glassware in pursuit of primarily constructive rather than analytical goals.

Paying careful attention to the novel ways in which chemists began to use glass from the early-nineteenth century onwards, and to their reasons for doing so, suggests that other aspects of the existing view of nineteenth-century chemistry warrant revision. For example, it shows that even where historians have been concerned with practical chemistry they have tended to overemphasise the post-Lavoisierian Parisian experimental tradition at the expense of the chemical practice of Berzelius, even though this was recognised by his contemporaries as highly influential. I trace the origins of this imbalance to the same historians' dominant interest in telling a progressive, theoretically-driven narrative, a historical approach which has resulted in the almost complete neglect of the difficulties of moving chemistry away from centres of *élite* practice.

The preceding chapters of this thesis discussed the effects of that outlook on our understanding of Liebig, but the increasing geographical dispersion of chemistry as an academic discipline during the early-nineteenth century means that such issues are of much more general importance to the history of chemistry. Relying on the professionalisation of chemistry, however this came about, to explain the growth of practical chemistry within the academic discipline and its spread to new locations gives no insight whatsoever into *how* chemists were able to do chemistry under these circumstances. Studying chemists' use of glass, on the other hand, highlights exactly the problems of geographical isolation and limited financial resources faced by so many nineteenth-century chemists and it shows how, in overcoming these difficulties, they reformed chemical practice around a new material culture.

This practice and its associated material culture in glass drew heavily on chemistry's artisanal and mineralogical roots, leading to a model of academic scientific practice which subverts long-held notions of the relationship between theory and experiment, and between scientists and technicians. Glass, in the hands of glassblowing chemists and scientifically-knowledgeable glassblowers, both encouraged highly personal, expert innovation through the one-off creation of bespoke items, and was used to produce relatively low-cost, modular components for standardised, routine operations. Not only was glassware, as the example of the *Kaliapparat* shows, essential for the development of large-scale institutional training in chemistry, but these qualities of glass also fuelled a period of intense experimental creativity. Chemists made increasing demands on the skills of specialist chemical glassblowers to realise their ideas and, meanwhile, the provision of standard laboratory glassware to increasing numbers of students offered glassblowers lucrative entrepreneurial possibilities. The success of firms including Geissler and Gerhardt in Bonn, and Desaga in Heidelberg, rested on the glassblower's situation at the heart of the nexus of training and research constituted by late-nineteenth century chemical institutes.

The development of organic analysis in Giessen is acknowledged to have been inseparable from its institutional setting but I suggest that the institutional context (discussed in Chapter Five) was even more important to the emergence of organic synthesis. At least as much as analysis, I assert, synthesis depended on very large volumes of work carried out by highly trained practitioners within specialised laboratory spaces, but as I have shown it also depended on the introduction of many new experimental techniques. As a result, although some fundamental aspects remained constant – including learning to use the *Kaliapparat* – chemical training

was adapted to incorporate synthetic procedures involving the use of an increasing diversity of glassware, other apparatus and chemicals. Chemists' immediate surroundings were altered by these changes, but I propose that the new practice of synthetic chemistry had much more far-reaching consequences.

Everything from the design of the laboratory bench to the architecture of the building was affected by the shift from analytical to synthetic organic chemistry and I assert that these material developments, although they have previously escaped historical notice, were every bit as important to the development of large-scale training in institutional chemical laboratories as Liebig's introduction of the *Kaliapparat*. Without them chemists' exploration of reactivity and constitution, and their pursuit of synthetic targets, would have been immensely more laborious and unimaginably more hazardous than was the case. In the following, concluding chapter I argue that the development of institutional chemical laboratories was essential to the growth and increasing dominance of synthetic organic chemistry in the late-nineteenth century.

# Chapter Five: Building chemical laboratories "from the foundations to the roof"[729]

> *I was given four bare walls instead of a laboratory.*
>
> *Justus Liebig (1833)*[730]

> *Besides I am still busy with improvements and new fittings in the laboratory ... All these arrangements take a terribly long time.*
>
> *August Hofmann (1847)*[731]

## Introduction

The preceding chapters have addressed a series of central questions in the development of organic chemistry during the nineteenth century. They cover a period spanning more than half the century, and they follow organic chemistry from Paris to Giessen and beyond. Yet despite this temporal and geographical diversity, these chapters are united by their focus on chemistry as an inescapably *experimental* science. Each one has been concerned with the daily working practices of chemists, and they have all emphasised the wide range of resources chemists brought to bear on the problems they faced. This approach has consistently highlighted work, training and materiality – facets of chemical practice which, though scarcely controversial, are nevertheless frequently ignored or suppressed in accounts whose main goal is to relate the development of chemical theory. By recovering the effort, skill and sheer physicality of chemical practice, this dissertation has begun to show what nineteenth-century organic chemists were actually doing in the laboratory, and in this concluding chapter I argue that these same factors transform our understanding of the laboratories in which those chemists worked.

The early chapters of this dissertation re-examined Liebig's development of large-scale training for chemical research in Giessen, a change which placed new demands on the laboratory environment. By 1833 (see epigraph) Liebig was feeling the limitations of his original laboratory, but it was not until the late 1830s that he was granted sufficient funds to address its shortcomings. Then Liebig, together with the architect Paul Hofmann,[732] undertook a major reconstruction of the Giessen

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[729] Wurtz 1882, 7.
[730] Justus Liebig to Justin Linde, Chancellor of the University of Giessen, 12 August 1833. Cited in Brock (1997, 59).
[731] Hofmann to Liebig, 4 February 1847, in Brock 1984, 66.
[732] Paul Hofmann was state architect of Hessen-Darmstadt and father of August Hofmann. To avoid confusion, I have referred to Paul Hofmann throughout, only using Hofmann to refer to August Hofmann.

barracks building housing Liebig's school, adding an extension for the new analytical laboratory.[733] This laboratory, completed in 1839, was where Blyth and Ortigosa analysed coniine, and it was the site of Muspratt and Hofmann's first *synthetical experiments* (Chapter Three). At the time it was built, it represented the state-of-the-art in laboratory design and construction, widely publicised by means of Paul Hofmann's 1842 book and accompanying series of woodcuts.[734]

Such has been the power of the *Giessen Model* that historians have tended to overlook developments in the laboratory space after Liebig, thereby tacitly endorsing the view often expressed by chemists that Liebig's Giessen laboratory continued to serve as a physical model for academic chemical laboratories during the remainder of the nineteenth century and into the twentieth.[735] The buildings housing chemical laboratories may have got a lot bigger but – in the absence of historical studies to the contrary – we are left to assume that the laboratory itself remained essentially the same.[736] Examining the three figures (20, 21 and 22) reveals the inadequacy of this view. Indeed, there are ways in which Liebig's laboratory is much more similar to the eighteenth century chemical laboratory than it is to the late-nineteenth century teaching laboratory. The Giessen laboratory was an open communal space, in which chemists jostled for space at tables and benches. Like the earlier chemical laboratory it was crowded and untidy, the floor strewn with equipment, precarious assemblies of apparatus covering every surface. The late-nineteenth century laboratory, by contrast, was a highly organised space. In addition to certain communal areas, such as the fume cupboards, each chemist was provided with his own workspace, a carefully designed, well-lit bench supplied with gas and water, a range of shelving and lockable cupboards for the storage of his reagents and equipment, and a metal scaffold for the secure support of complex assemblies of glassware. These images show that a great deal changed in the half-century after

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[733] Brock (1997, 57-61) discussed Liebig's growing dissatisfaction with the original laboratory provided in Giessen and the construction of his new laboratory.
[734] Hofmann's (1842a) book was published with an accompanying Atlas (Hofmann, 1842b).
[735] Fischer and Beckmann (1913, 7) made exactly this claim for the newly built Kaiser Wilhelm Institut for chemistry in Berlin.
[736] Historians of chemistry have generally restricted their interest to the laboratory before 1800. See, for example, Crosland (2005). Even Partington's (1942) summary, though it covered a more extended period, emphasised changes before about 1800.

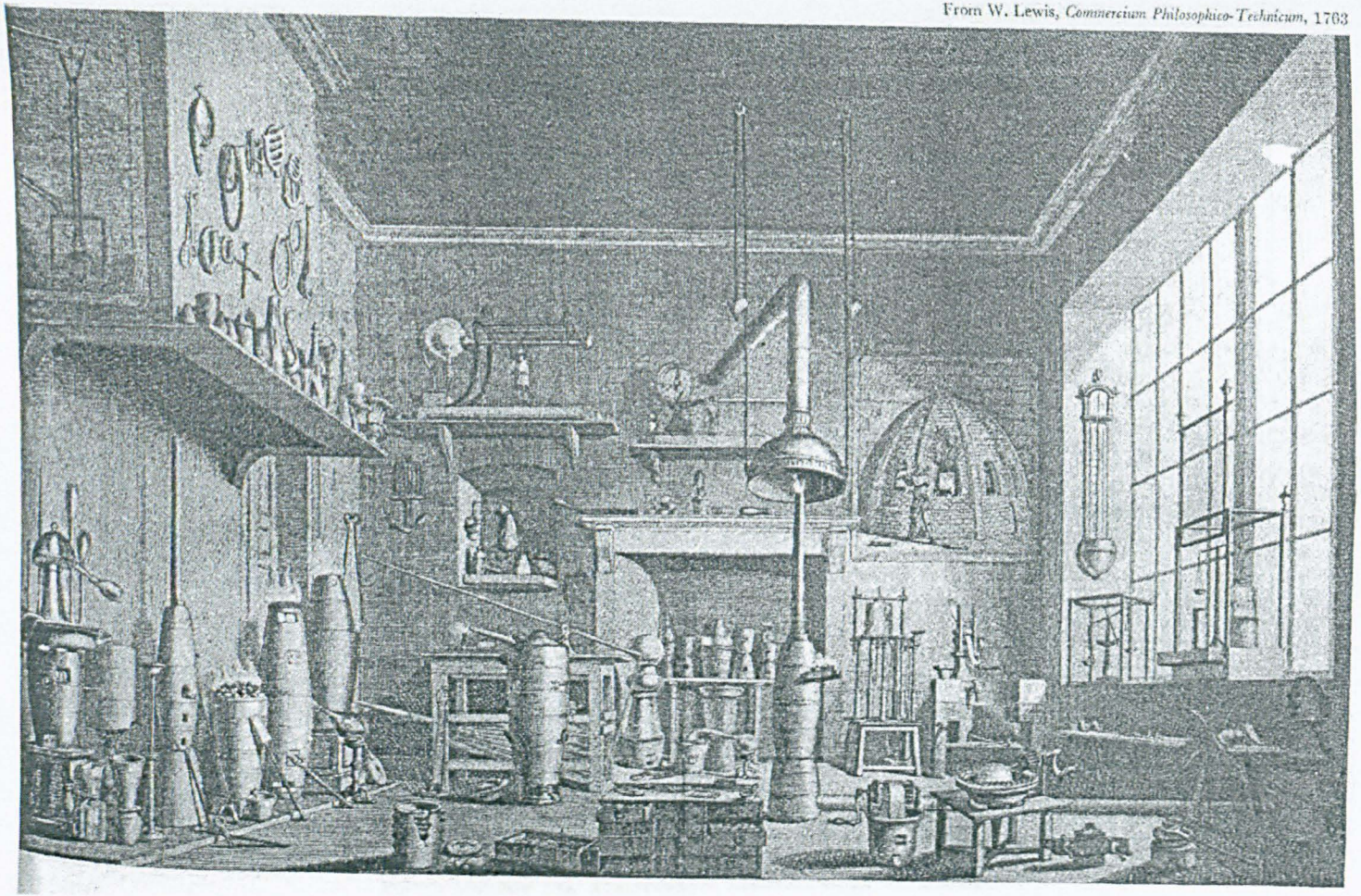


Figure 20. Late-eighteenth century chemical laboratory. W. Lewis, *Commercium Philosophico-Technicum*, 1763. Taken from Partington 1942, 147.

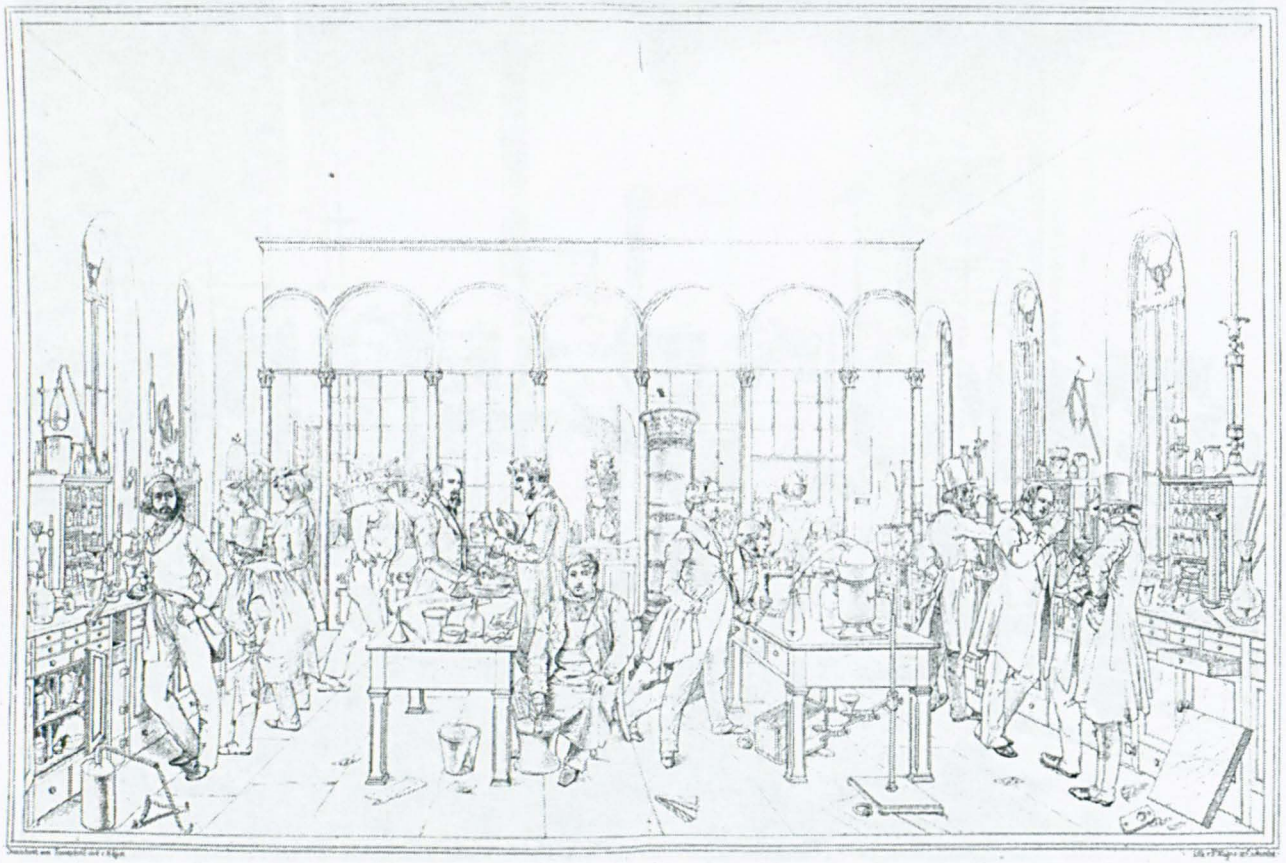


Figure 21. Trautschold's famous 1842 woodcut was included in the Atlas (1842b) accompanying Paul Hofmann's (1842a) description of Liebig's Giessen laboratory.

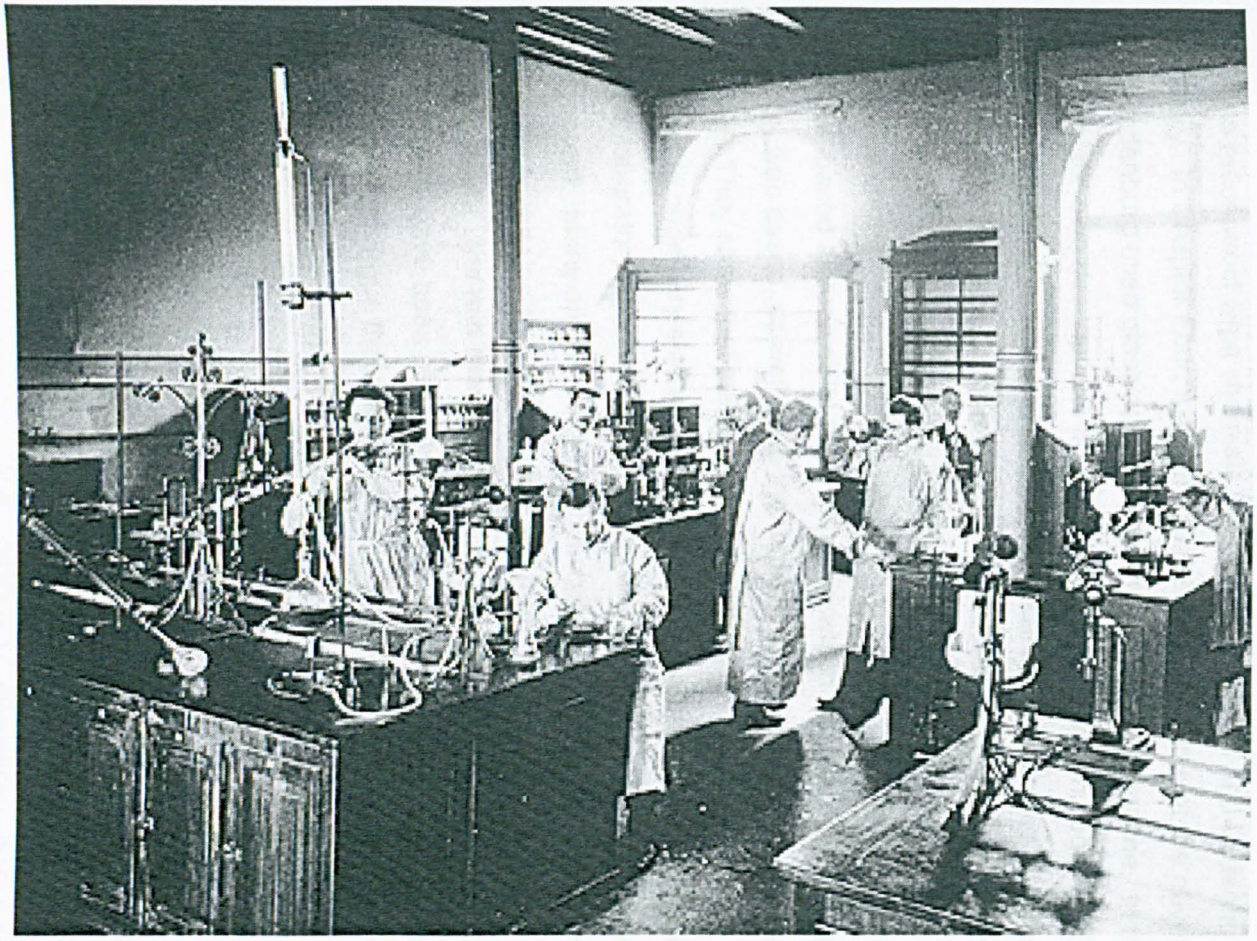

Figure 22. This photograph shows the chemical teaching laboratory in Stuttgart around 1900.
Taken from http://www.uni-stuttgart.de/ueberblick/geschichte/index.html (last accessed 18 September 2008).

Wilhelm Trautschold captured Liebig's laboratory in 1842, and they suggest that many important and extremely durable features of institutional chemical laboratories were developed during that period. The late-nineteenth century laboratory, I argue in this chapter, is a vastly better model for twentieth-century academic teaching and research laboratories than the Giessen laboratory.

In this dissertation so far I have used laboratory notebooks, textbooks and published papers to reconstruct what chemists like Liebig, Hofmann and Ladenburg did in the laboratory. In Chapter Four, for example, I examined some of the novel ways in which Ladenburg used glass apparatus in the synthesis of coniine. In this chapter I use chemists' own descriptions of laboratories built between about 1865 and 1900 to provide direct evidence for changing chemical practice during this period, and I argue that the development of training and research in synthetic organic chemistry went hand-in-hand with a new, purpose-built laboratory environment. These chemists' accounts refer directly to the immense scale of labour and novel glassware-based experimental methods upon which the practice of synthetic organic chemistry was based, as well as to the unpredictably hazardous new substances it produced. They show that teaching and doing organic synthesis posed numerous challenges to chemistry's academic credentials, and that chemists responded by using the laboratory to enforce a highly organised system of disciplinary management. Many eminent chemists devoted significant portions of their active working life to the design, construction and management of institutional chemical laboratories from the mid-nineteenth century onwards (see Hofmann's epigraph). They may well have been partly motivated by the desire for power, status and public recognition, but I argue that their work was also essential for the provision of a productive and acceptably safe laboratory environment for the new and rapidly expanding practice of synthetic organic chemistry.

## Building Magnificent Palaces

> *No scientific institute requires the fulfilment of so many and such various conditions in its design and arrangement as a chemical laboratory, and the difficulties arising out of this increase considerably with the number of students for whom practical instruction must be provided.*
>
> *Leopold von Pebal, 1880.*[737]

It had been common throughout the first half of the nineteenth century to create laboratories by re-fitting rooms originally designed and built for other purposes, but by the mid-1860s organic chemistry was testing the limits of such chemical

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[737] Robins (1887, 47) was Robins' translation of Pebal (1880, 5).

laboratories to breaking point.[738] According to Hermann Kolbe,[739] the Marburg laboratory he had inherited from Robert Bunsen in the late 1850s was so crowded and inadequately ventilated that the health of those working there was "perceptibly endangered". In 1863 Kolbe, together with the architect Regenbogen, was able to remove these deficiencies "through a radical remodelling and through extension" of the existing facilities.[740] Even so, working within the constraints of an existing building meant that Kolbe and Regenbogen could not fulfil certain aspects of contemporary best practice in laboratory design. They were unable, for example, to provide the main laboratories with overhead light in addition to the side windows, nor to group the work tables according to the best system throughout.[741]

Thus, although Kolbe declared himself "satisfied in general" with the outcome, his text also makes clear that chemistry was rapidly outgrowing the sort of laboratory which could be created within an existing building.[742] One factor in this was certainly the growth in student numbers but, as the epigraph to this section makes clear, catering for more students involved much more than merely building a *larger* laboratory. Where a large number of chemists were to work together, and particularly where many of these were students in training, the provision of the most suitable possible laboratory environment intersected with a whole series of issues relating to chemical pedagogy and practice. How should the layout of the laboratory building reflect the various modes and levels of training? What facilities were required or made desirable by recent developments in experimental technique? In other words, how could the physical organisation of the laboratory best support and reinforce chemistry's new disciplinary structure?

The most famous chemical laboratories built during the 1860s are undoubtedly those built for Hofmann at Bonn and Berlin (Figure 23). They are also amongst the best documented, thanks in part to the extensive report on their design and construction commissioned from Hofmann by the British Department of Science and Art.[743] In the remainder of this section, I use Hofmann's report together with other largely published sources to show how chemists and architects worked together to address the issues just raised concerning laboratory design. I have structured this

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[738] See the description in Faraday 1827.
[739] For more details on Kolbe, see Rocke's (1993b) biography.
[740] Kolbe 1865, 7.
[741] Ibid., 8.
[742] Ibid., 8.
[743] Hofmann 1866. Hofmann's new laboratories were also discussed by William Crookes in *Chemical News* (1868) **43**: 215-216.

Fig. 9.

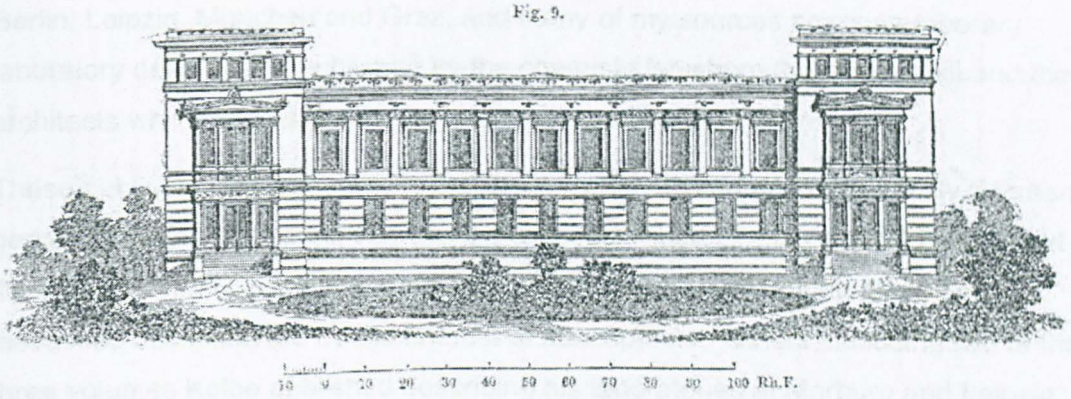


Fig. 17.

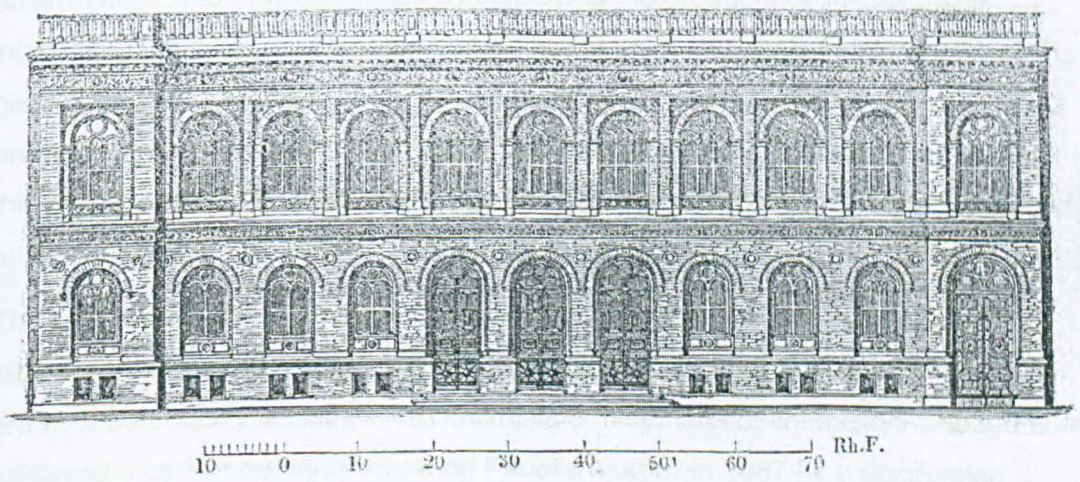


Figure 23. The great chemical laboratories at Bonn (above) and Berlin (below) were both built under Hofmann's direction. Hofmann 1866, 316 and 340.

material in a series of short sub-sections, at the end of which I summarise the relationship between pedagogy, practice and the laboratory towards the end of the nineteenth century. I concentrate mainly on the great laboratories built in Bonn, Berlin, Leipzig, München and Graz, and many of my sources are contemporary laboratory descriptions published by the chemists for whom they were built and the architects who designed them.

These published primary sources belong to a little studied and distinctively German genre.[744] Some examples, such as the architect Albert Cremer's 1868 book about the laboratory built in Berlin for Hofmann, consist mainly of ground plans and elevations accompanied by the briefest of descriptions. Others, including two of the three volumes Kolbe published describing his laboratories at Marburg and Leipzig, are in a different mould. Proceeding from a detailed description of the laboratory, accompanied by architectural plans for the building and diagrams of its internal fittings, Kolbe devoted considerable space to explaining the principles and methods by which chemistry was being taught in his laboratories. These books set out Kolbe's understanding of how pedagogy and practice related to the laboratory environment, and they concluded by displaying the products of successfully integrating the three: published research produced in the institution by the director, his students and assistants.[745] Kolbe's books, and others like them, show that the productivity of an institutional chemical laboratory was directly affected by the way that chemistry was taught and practised within, and that the laboratory itself played an important role in managing both pedagogy and practice.

The chemist Leopold Pebal's 1880 book (see epigraph) describing his new laboratory at Graz also warrants a special mention. Neither Pebal nor his institute are now particularly well-known to chemists or historians of chemistry – though both achieved a certain notoriety following Pebal's murder in 1887 by a disgruntled former employee on the very steps of the institute – but the book and the building are nevertheless important to this study.[746] Pebal began making plans for his institute from the early 1870s and, as part of this process, he analysed the relationship between the disciplinary structure of chemistry and the physical structure of its institutions. Pebal devoted almost a decade of his career to the design and construction of the Graz institute, which he believed represented the

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[744] I am using Germany and German here as collective terms referring to the German-speaking lands.
[745] Cremer, 1868; Kolbe, 1865; Kolbe 1872. Kolbe's earlier (1868) book about the Leipzig institute consisted mainly of the architectural plans.
[746] See Hofmann's (1887) report on Pebal's death.

state-of-the-art in laboratory building. He examined every aspect of laboratory building, comparing different approaches adopted elsewhere in Germany, selecting what he considered to be existing best practice and incorporating these ideas into his own design. His Graz institute is therefore a valuable snapshot of the laboratory building around 1880. Even more important for the present work, his book contains a unique, contemporary comparative study of chemical laboratories written from the perspective of a German chemist.

Comparative studies of German laboratory building were published in other European countries during the 1870s and 80s. As Hofmann's report shows, the British were very much interested in Germany's new institutional chemical laboratories, even before they were built. In the early summer of 1871, shortly before the completion of the Science Schools which became the Royal College of Science, an assistant director of the South Kensington museum Captain Festing spent a month in Germany visiting laboratories.[747] Around the same time the chemists Adolphe Wurtz and Giorgio Roster made similar fact-finding tours, inspecting laboratories, interviewing chemists and accumulating plans. Both men published comprehensive reports of what they discovered, and their analyses of Germany's growing command of chemistry in general, and organic chemistry in particular, were evidently intended to stimulate their governments (French and Italian, respectively) to action.[748]

In Britain, interest modulated into concern in the decade following Festing's visit, and in 1882 the laboratory architect Edward Cookworthy Robins volunteered to accompany a party led by the chemist Henry Armstrong and the physicist William Ayrton on an extensive tour of German institutions for scientific research and training.[749] When Robins' comprehensive report on laboratory construction was published in 1887 it set out a heartfelt plea for training in "intelligent doing, the result of artistic practice and scientific understanding". According to Robins, this was the only way for Britain to maintain and improve her standing in relation to other, rapidly industrialising European nations and, although Robins couched his pleas in general terms relating to "Technical Education" and "foreign nations", his "Comparative

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[747] Festing 1871.
[748] Wurtz (1870); Roster (1872). See also Wurtz' second report (1882).
[749] Robins 1887, 17. The party was sent from the Executive Committee of the City and Guilds of London Institute for the advancement of technical education, of which Robins, Armstrong and Ayrton were all members.

Analysis" was overwhelmingly focused on Germany's institutional chemical laboratories.[750]

Robins envisaged his work as a contribution to contemporary British educational debates but it is more important for the purposes of this study that his work also provides an invaluable synoptic view of late-nineteenth century laboratories and a most instructive insight into how purpose-built laboratories were perceived *at the time* to be important tools in controlling the disciplinary development of chemistry.[751] In 1885 a report on the "magnificent series of palaces" which constituted the new university at Strasburg prompted the deeply frustrated Editor of *Nature*, the astronomer Norman Lockyer, to rail against the "astounding neglect and apathy that have prevailed and still prevail" in Britain.[752] A detailed comparison of British and German chemical laboratories might be expected to shed light on why organic chemistry became such a predominantly German science in the late-nineteenth century. Such an investigation lies well beyond the scope of this dissertation. But by demonstrating the extent to which purpose-built institutional laboratories were *functional* parts of the apparatus of nineteenth-century German organic chemists, enormous and expensive but nonetheless essential components of their chemistry set, this study suggests why it became all-but impossible for chemists elsewhere to participate in the development of synthetic organic chemistry during the late-nineteenth century.

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[750] Robins 1887, 1-3.

[751] Cardwell (1972) remains the classic study of nineteenth-century British technical and scientific education. Bud and Roberts (1984, Chapter Three: "Visions in institutional form") described the development in Britain of advanced training in chemistry during the nineteenth century, principally at a number of colleges outside the university system including the Royal College of Chemistry and University College in London, and at Owens College in Manchester. On the role of chemistry as the basis for a liberal education within the late-nineteenth century British university, see also Roberts 1980.

[752] This description is taken from Robins (1887, 65) and was based on "The new university of Strasburg", *Nature*, April 16 1885, 557-562. See also, Editorial, *Nature*, April 16 1885, 549-550. The founder and Editor of *Nature*, Lockyer had been appointed Secretary of the Royal Commission on Scientific Instruction and the Advancement of Science [the Devonshire Commission] in 1875.

## Institutionalising a "chemical atmosphere"

> *The good arising from a large number of students working together in an extensive institution is unmistakable. If the student have but his eyes open to the work of his neighbours he has opportunities of gaining, in a comparatively short time, an amount of experience which, working alone or in company with only a few, he could scarcely gather during years of diligent labour. It is the chemical atmosphere in which he works that promotes his progress.*
>
> *August Hofmann (1866)*[753]

Liebig's Giessen laboratory helped to establish a fundamental and durable principle in the practical training of chemists: students and assistants worked together in a communal laboratory. This arrangement had many benefits. Students could learn from watching others performing operations in which they were not yet expert, and they had ready access to the assistance of more experienced chemists. Skills could be developed and shared within this learning community without the immediate involvement of the director, a division of labour which was – as I discussed in Chapter One – essential to its success and productivity. At the same time, the director retained complete oversight of the work of the laboratory, with the result that he also maintained that control which is so necessary to the establishment and development of a discipline. What I shall call the principle of directed, communal training remains important today, even though the greater sophistication and specialisation of modern chemical training mean that its implementation has become considerably more complicated than anything Liebig or his contemporaries envisaged.

As early as the 1840s the new laboratory at the Royal College of Chemistry (RCC) in London, whose layout was designed by Hofmann in consultation with his former teacher Liebig,[754] incorporated separate designated spaces within the laboratory for beginners learning the rudiments of qualitative analysis, and those more advanced students who were occupied with quantitative organic analysis and a range of other chemical operations.[755] During the mid-century organic chemistry expanded to include additional analytical and preparative procedures, including Hofmann's own *synthetical experiments* and – eventually – the new methods of constructive

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[753] Hofmann 1866, 299.

[754] A meeting of the Council of the newly founded RCC heard that the architect "Mr Lockyers plans have been examined and approved by Prof Liebig and Dr Hofmann". Minutes of the Council of the RCC, 15 September 1845 (Imperial College Archive, C3/566). Hofmann also discussed the arrangement of the temporary laboratory at the RCC in his first letter to Liebig following his arrival in London. See Brock 1984, 36: Letter 10, undated [October? 1845]. Laboratory matters featured heavily in much of their early correspondence.

[755] Armstrong (1896, 690) described "the bench at which the seniors worked being in front of the upper row of windows" of Hofmann's Oxford Street laboratory.

synthetic organic chemistry. Learning to perform quantitative analyses using the *Kaliapparat* necessarily remained a central aspect of basic training in organic chemistry but it was rapidly supplemented by a variety of other practical techniques learnt and applied by more advanced students.[756]

Hofmann's 1866 account of the Bonn laboratory (see epigraph) confirmed the value of communal laboratory practice but it also explained why, without sufficient direction, it could be counterproductive. As Hofmann continued:

> *These advantages, on the other hand, cease when the number of learners exceeds those limits within which personal supervision is still possible. As soon as the beginner is no longer conscious that he is able to procure help at any moment; as soon as the more advanced student feels no longer that he receives individual attention; lastly, as soon as the young chemist, though working independently, is no longer satisfied that an experienced eye watches over his steps, the chemical institution, however excellently it may be organized in other respects, will yield very indifferent results indeed.*[757]

In Bonn 60 permanent workspaces were evenly divided between three principal teaching laboratories, 20 being the maximum number of students Hofmann believed could be supervised for any length of time by a single assistant. Thus beginners, advanced students and young chemists each shared a laboratory with their peers, thereby combining what Hofmann considered the optimal organisation of the physical space of the building as a whole with the best possible disciplinary management:

> *Not only was it possible to fit up each laboratory in a manner suitable to the wants of each particular class, but the situation of the rooms themselves could be so adapted to the remaining parts of the building as to offer the greatest facilities to each division. And higher still must be rated the advantages as regards readier supervision and increased means of maintaining discipline in all parts of the institution afforded by an arrangement of this kind.*[758]

The application of this pedagogical principle was important in determining how many large teaching laboratories were contained within an institute building, and how different kinds of work were allocated to those spaces. The Bonn laboratory was somewhat unusual in having three such laboratories, but many laboratories built in Germany during the 1860s and 70s adopted Hofmann's plan of devoting separate laboratories to qualitative and quantitative analysis, and providing separate space for research. For example, both Kolbe's Leipzig institute and Baeyer's extensively

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[756] See, for example, Kolbe's (1865, 24-25) description of how the introduction of preparative chemistry was changing practical training.
[757] Hofmann 1866, 299.
[758] Ibid.

remodelled München laboratory were constructed on the principle of allocating separate laboratories to beginners and advanced students.[759]

Pebal was one of the few dissenters from this view. Writing a year after the opening of his new Graz institute in 1879, Pebal argued that:

> *The incitement to work which a laboratory offers is proportionate to the varied character of the work which is carried on in it. Improved planning and arrangement, as well as good methods of ventilation and sufficient superintendence, have tended to lessen the difficulties of carrying out different kinds of researches at the same time and place.*[760]

Unlike Hofmann, Pebal preferred to integrate the teaching of qualitative and quantitative analysis, a choice he considered to be made viable in part by improvements in laboratory building. Pebal's decision was reflected in the design of his institute: there were two main teaching laboratories but these could be used flexibly, allowing beginners to work alongside advanced students. One advantage of this arrangement was that students could be evenly distributed between the two laboratories, thereby avoiding overcrowding in one room whilst the other was almost empty. But Pebal's decision had other consequences for the arrangement of subsidiary rooms within the institute, including the provision of some smaller rooms for the exclusive use of advanced students so that they could leave apparatus set up for longer periods, and some space available to all students for the execution of operations requiring a large amount of room.[761]

These institutes show that pedagogy and practice were inseparable from laboratory design and construction in the late-nineteenth century. The principle of directed communal training was widely accepted, but chemists had varying opinions regarding its implementation. These pedagogical decisions, moreover, not only had a direct effect on the arrangement and internal fitting of an institute but were also limited by the technical constraints of building. I therefore argue that the development of chemical training and research during this period went hand in hand with a new laboratory architecture whose purpose was to optimise the management of ever-larger numbers of students and an increasing variety of experimental techniques.

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[759] Hantzsch (1909, 76) on Leipzig; Robins (1887, 51) on München.
[760] Robins' (1887, 48) translation of Pebal (1880, 6).
[761] Robins 1887, 48; Pebal 1880, 6.

## Large-scale Training, Discipline and Laboratory Safety

> *I consider it moreover very much essential, that different work rooms be present for different purposes, above all particular rooms for the first analytical beginners who, as yet inexperienced, are generally the least careful and cautious in the manipulation of substances which spread foul smelling or damaging fumes*
>
> *Hermann Kolbe (1865)*[762]

> *Nothing is easier than to equip a room for the use of only a small number of chemistry students. But where many are supposed to work together, the arrangement requires the most careful consideration. [...] Anyone who has run a laboratory for long knows that there are some people who are extremely difficult to convince that they should use these fume extractors without fail, despite repeated advice and even where the fume extractor is only a few steps away.*
>
> *Hermann Kolbe (1872)*[763]

I have already mentioned that Kolbe's Leipzig laboratory followed Hofmann's plan of providing separate laboratories for chemists at different stages of their training. But whereas Hofmann justified this arrangement entirely on grounds of its pedagogical superiority, Kolbe's epigraphs show that there was more at stake than the efficiency and productivity of the institution. Kolbe, whose Leipzig institute housed more than four times the number of students as his earlier Marburg laboratory and more than twice as many as Hofmann's new Bonn laboratory, acknowledged that part of the problem was to make sure that each student had enough space and easy access to the necessary apparatus and services.[764] But it was equally important to ensure that: "there is a room with an efficient extractor near every workbench, in which substances producing volatile, terrible-smelling or damaging fumes can be handled". Even where such facilities were available, Kolbe lamented (see epigraphs), it was often difficult to persuade people to make the small effort required to use them.[765]

Kolbe's concerns show that aspects of chemical practice challenged the viability of larger laboratories by making them unsafe places of work. Such challenges, moreover, were greatly intensified where inexperienced chemists who often failed to appreciate the possible consequences of their actions were performing potentially dangerous operations. In these circumstances it was essential that students were encouraged to follow correct procedures by all possible means, and these included

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[762] Kolbe 1865, 8.
[763] Kolbe 1872, XIX-XX.
[764] Kolbe was called to Leipzig almost immediately following the publication of his description of the Marburg laboratory, where a new chemical institute opened in 1868 was built for him. See Kolbe 1872, VII. Whereas the Marburg laboratory had accommodated about 30 students, Kolbe's Leipzig laboratory had space for 100 and was rapidly updated with places for 30 more. See Kolbe 1865, 10-11; *idem.* 1872, XVIII-XIX.
[765] Kolbe 1872, XIX-XX.

the best arrangement of the various rooms and shared facilities of a modern laboratory as well as rigorous training. Discipline was therefore a vital component in maintaining the safety as well as the productivity of the laboratory, and this discipline was partly achieved through laboratory design and organisation.

Optimising laboratory ventilation, for example, had implications for the design of the building as a whole. As Robins explained:

> *The fittings are not independent of the structure in science laboratories, but in most cases are an integral part of it. The heating and ventilation alone necessitate the preconception of what provision is to be made in the solid walls or floors for the admission or extraction of fresh and fouled atmosphere, which provision must be in the neighbourhood of the fittings wherein the noxious fumes are generated; and the system of withdrawal from these must be in the same direction as that of the general room ventilation, which is of course simultaneously going on.*[766]

One consequence of this was that chemists should be involved in the design of new laboratory buildings from the earliest possible moment. As Robins warned the British, "nothing is so fallacious as the system too often adopted of consulting the professor about the fittings only after the building has been erected".[767] In Germany, by contrast, it was usual for the professor to retain ultimate control over the design and construction of the laboratory, the architect being required to adjust his "artistic intentions" to the chemist's "more practically directed wishes".[768] Although Britain and Germany prioritised the expertise of the chemist and architect differently, successful laboratory building was understood in both countries to be the product of close collaboration between the two.

## Light, Air and Location

> *Thus, unfettered by narrowness of space, or the prospect of having air or light shut out by the close proximity of other buildings, the architect was enable to lay out the plan of the edifice with a degree of freedom that has materially promoted the beauty and harmony of his work.*
>
> *August Hofmann (1866)*[769]

The Bonn laboratory whose advantages Hofmann described (in the epigraph) was built around four courts (Figure 24), an arrangement which was adapted in Kolbe's e-shaped institute at Leipzig and in Pest, where the laboratory took the form of a "p".[770] Particularly on open sites, layouts of this kind offered many advantages,

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[766] Robins 1887, 3.
[767] Ibid., 111.
[768] Kolbe (1868, XVI) described the architect Zocher's unusual willingness to accommodate Kolbe's wishes. Hofmann (1866, 293 and 325) was similarly complimentary about the work of the architects Augustus Dieckhoff in Bonn and Albert Cremer in Berlin.
[769] Hofmann 1866, 294.
[770] Pebal 1880, 6.

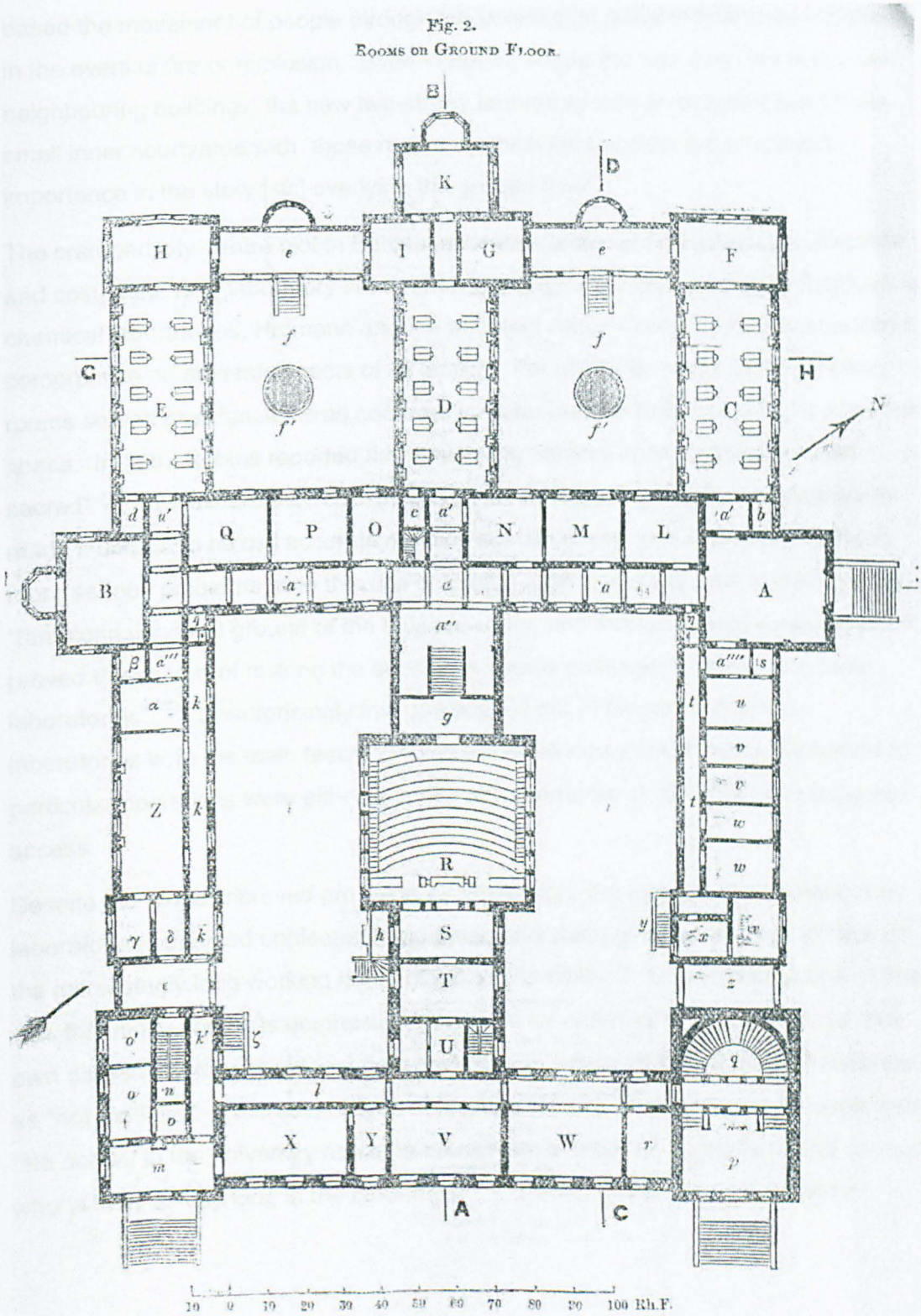


Figure 24. Hofmann's Bonn laboratory was arranged around four courts in order to maximise light and air. Most late-nineteenth century chemical laboratories were built around one or more internal courtyards. Hofmann 1866, Fig. 2.

eased the movement of people through the building, to potentially life-saving effect in the event of fire or explosion. Even in Berlin, where the site was flanked by tall, neighbouring buildings, the new two-storey laboratory was arranged around three small inner courtyards with "those rooms in which light and air are of primary importance in the story [sic] overlying the ground floor".[771]

The cramped city-centre plot in Berlin meant that, although the grandeur, elegance and cost of the new laboratory set a new standard for the construction of institutional chemical laboratories, Hofmann and the architect Albert Cremer nevertheless had to compromise on several aspects of its design. For example, many of the smaller rooms served dual functions as corridors in order to maximise the use of limited floor space. In 1887 Robins reported that: "even the balance-room [in Berlin] is not sacred".[772] The disturbance caused by people moving through the balance-room made it difficult to record accurate masses but there were other, potentially much more serious problems, with this use of space. During Robins' visit to Berlin, a fire "ran along upon the ground of the balance-room, and though speedily extinguished, proved the danger of making the subsidiary rooms passages between the main laboratories".[773] Unsurprisingly this practice fell out of favour, and in later laboratories both the main teaching rooms and the many small rooms dedicated to particular operations were either reached from corridors or had their own separate access.

Despite the much improved provision for ventilation, the atmosphere in these new laboratories remained unpleasant and potentially damaging, particularly in view of the increasingly long working hours of junior chemists.[774] One consequence of this was that many chemists emphasised the need for chemical institutes to have their own garden. Kolbe considered the small garden adjoining the director's residence as "not the least" of the advantages of his new Leipzig laboratory. As he explained, "No *docent* in the university needs to recuperate in fresh air so badly as the chemist, who is busy all day long in the laboratory".[775] Hofmann was also proud of the

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[771] Hofmann 1866, 326. These rooms included the two main teaching laboratories, the director's private laboratory and the lecture theatre, as well as a number of subsidiary smaller rooms (pp. 331-334).
[772] Robins 1887, 49.
[773] Ibid., 50.
[774] The introduction of gas light in the 1860s made it possible for chemists to work in the laboratory after dark. See, for example, Kolbe 1865, 11.
[775] Kolbe 1868, 28.

"handsome garden" surrounding his Bonn laboratory, although no similar provision was possible on the limited site of the Berlin laboratory.[776]

Gardens, particularly botanic gardens, had previously been associated with chemical laboratories because of the links between pharmaceutical chemistry, botany and medicine. By the late-nineteenth century these disciplinary links had been somewhat marginalised by chemistry's rising status and independence, and by its much-publicised connection to new industries and their associated wealth.[777] Even within the academic context, however, doing chemistry remained dirty, smelly and dangerous, with the result that its grand new institutes were frequently exiled to semi-rural sites on the periphery of the built-up area.[778] There they were soon joined, not only by companion scientific institutes such as those for physics and physiology but also by relocated university botanic gardens, leading to the creation of the suburban scientific-medical university districts typical of so many German cities (Figure 25).[779]

## Tempering the Wind

> *In the same way the special ventilation for chemical laboratories requires both common-sense and care, for many otherwise admirable systems have failed in consequence of the neglect of obvious requirements – till too late to amend them – chiefly arising from the want of a complete understanding between the architect and the ventilating engineer or the professor himself.*
>
> *Edward Cookworthy Robins (1887)*[780]

Robins' epigraph suggests that the provision of good laboratory ventilation was particularly sensitive to the quality of communication between the architect and the chemist (or engineer). It was a tricky problem, only effectively solved in buildings dating from around 1880, such as Pebal's institute at Graz and the laboratory built for Professor Landolt at Aachen Polytechnic, where both the system of general ventilation and the extraction of fumes through a variety of smaller, dedicated laboratory fittings were mechanically driven. Shortly after his Graz institute was

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[776] Hofmann 1866, 294.
[777] Both Hofmann (1866, 293) and Kolbe (1868, 1) referred to the important relationship between academic chemical laboratories and industrial development.
[778] Hofmann's experiences in London illustrate the difficulty of situating a chemical laboratory in a densely populated, urban area. Complaints from neighbours of the RCC were a recurring problem, especially in its temporary accommodation. Minutes of Building Committee, 18 February 1846, (C3/566 Imperial College Archive).
[779] Leipzig was a particularly early example of this trend. See Kolbe 1872, XIV; 1868, 4.
[780] Robins 1887, 45.

Fig. 1.
Situationsplan.

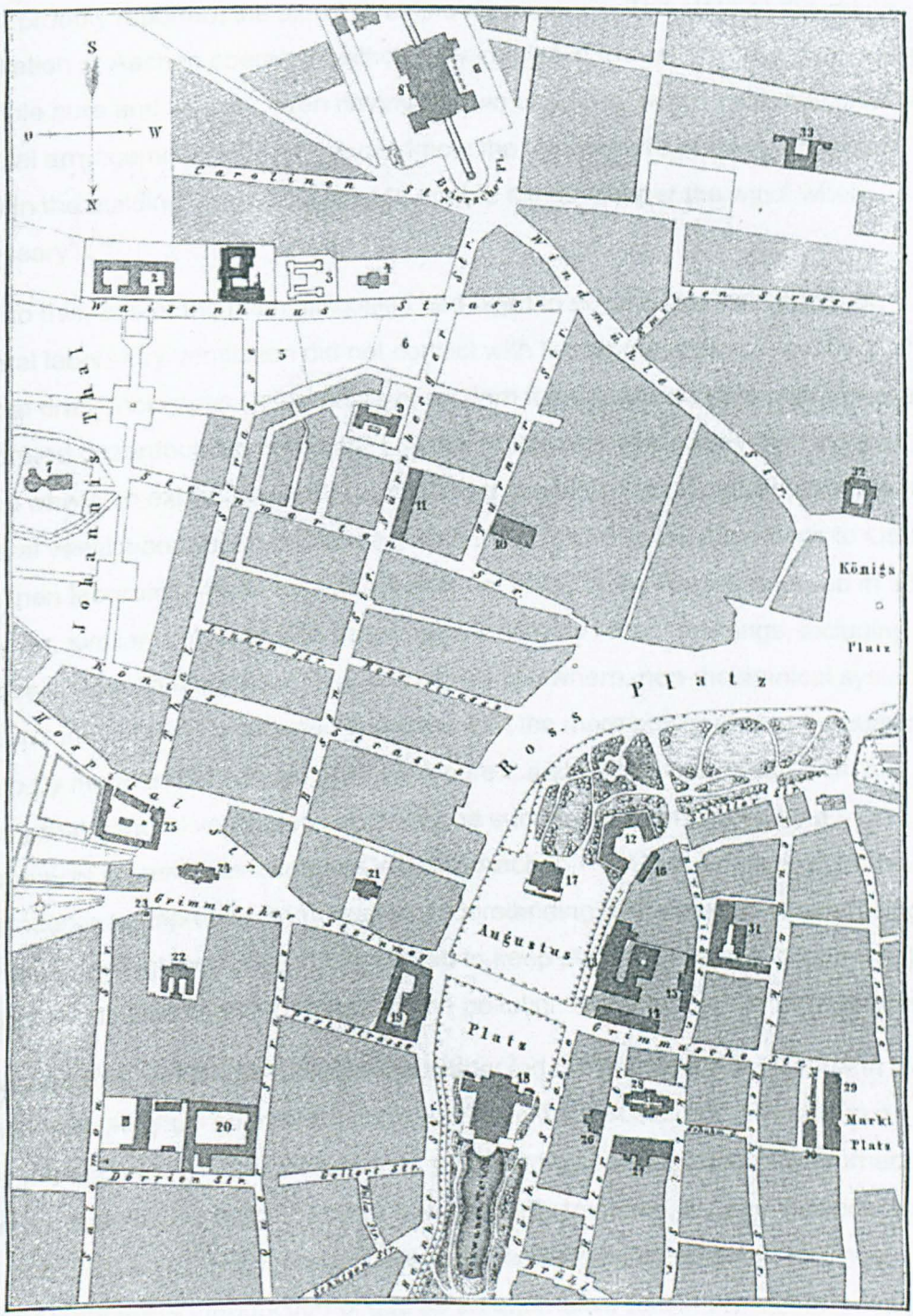


Figure 25. Kolbe's (1868, Fig. 1) Leipzig laboratory (1.) was situated on the outskirts of the city, flanked on either side by the new hospital (2.) and the physiological institute (3.).

completed, Pebal filled one of the main laboratories with thick clouds of ammonia and set the fan driving the ventilation system to rotate quickly. Within half an hour, Pebal proudly reported, the air was completely clean.[781] The state-of-the-art installation at Aachen operated "without any conflict in the action – the *push* and *pull* principle pure and simple", even having its own engineer "who has an electrical tell-tale dial arrangement by which he can know the temperature of every important room in the building, and appliances to enable him to 'temper the wind' when necessary".[782]

Prior to this, one of the main difficulties had been to ensure that the system of general laboratory ventilation did not conflict with the air currents created by the special draft enclosures (forerunners of modern fume cupboards) in which chemists performed hazardous experiments. The risk of this was particularly high in rare cases where an existing laboratory was being modified – as, for example, when the general ventilation system had to be switched off following the alterations to Liebig's München laboratory made for Adolf Baeyer in 1875.[783] As Robins reported in 1887, however, similar problems also beset many relatively recent buildings, including Carl Graebe's Geneva laboratory. In Geneva and elsewhere, non-mechanical systems of general ventilation were unable to cope with the more powerful counter-currents set up by mechanically driven draft enclosures, and Robins concluded from his survey that general ventilation could only be successful when driven by a mechanical system – as it was in Graz and Aachen.[784] Although general laboratory ventilation was improved by increased understanding of the means of controlling the flow of air through buildings, it often failed to keep pace with innovations in smaller, specialised fittings intended to reduce the pollution of the laboratory atmosphere.

Poor air quality in Liebig's Giessen laboratory led the architect Paul Hofmann to provide simple glass enclosures, believed to be the first such installations in a teaching laboratory.[785] Exhaust fumes produced by burning coke in the furnaces used for quantitative organic analyses were partly to blame, as was the widespread use of sulphuretted hydrogen (*Schwefelwasserstoffgas*) in inorganic analysis. August Hofmann's introduction of gas as an alternative fuel in the laboratories at the

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[781] Pebal 1880, 13. Pebal was replicating a test performed by Kolbe (1871, 31) in Leipzig.
[782] Robins 1887, 54.
[783] Ibid., 52.
[784] Ibid., 46.
[785] These enclosures were described in Carl Wilhelm Bergemann's report to the Prussian Minister on the chemical laboratory at Giessen in 1840, included as Appendix I in Brock (1997, 333-341). See also Jackson 2006, 293. These enclosures, visible on Trautschold's wood-cut, were also described by Hofmann (1842a, 3).

RCC was a partial solution to one of these problems but, as I have discussed elsewhere, Hofmann found that both the "increasing number of pupils, and the greater variety of operations performed by the more advanced students" created new challenges to laboratory ventilation.[786] Hofmann worked hard to address these problems at the RCC, although lack of funds and the restrictions imposed by an existing laboratory building severely limited what he was able to achieve.[787] It nevertheless seems reasonable to infer that these difficulties played an important role in developing Hofmann's understanding of the problem of laboratory ventilation. Certainly, Hofmann introduced much improved enclosures or closets into the new laboratories at Bonn and Berlin in the 1860s, using gas burners to draw air from the main laboratory through the closet.[788]

Hofmann's evaporation closets (*Abdampfnische* – see Figure 26[789]) and slightly larger draught closets (*Verbrennungsnische*) became standard features of many laboratories, including Kolbe's laboratory at Leipzig and Pebal's Graz institute.[790] They were situated between the window pillars, and enclosed between the external windows and internal sashes so that they were well lit.[791] Captain Festing, assistant director of the South Kensington museum, reported in 1871 that this arrangement enabled students to "keep all their apparatus entirely in the closet when at work", removing any need to bring apparatus into the open to examine it.[792] But Festing also discovered that not all chemists shared this concern for the health of those working in their laboratories. At the new Polytechnic in München, "Dr. Erlenmeyer pointed out to me that it was a great thing to have the sashes of the closets made to open so high that a student can work with his head inside the closet (or partially inside)".[793]

These installations largely solved the problems arising from small-scale laboratory work but larger operations continued to expose chemists to serious risks. As Pebal

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[786] Hofmann (1854) described the introduction of the gas furnace. See Minutes of General Meetings, 31 August 1846, 5 June 1848, and 3 June 1850 (C5/564 Imperial College Archive) for the direct quotation. Some of the steps Hofmann took to improve laboratory ventilation at the RCC are discussed in Jackson 2006, 304-305.
[787] Jackson (2004) examined these efforts in more detail.
[788] Hofmann 1866, 332.
[789] Cremer 1868, 4.
[790] Pebal 1880, 18; Kolbe 1868, XXII-XXIII.
[791] Cremer 1868, 4.
[792] Festing 1871, 6.
[793] Ibid., 13.

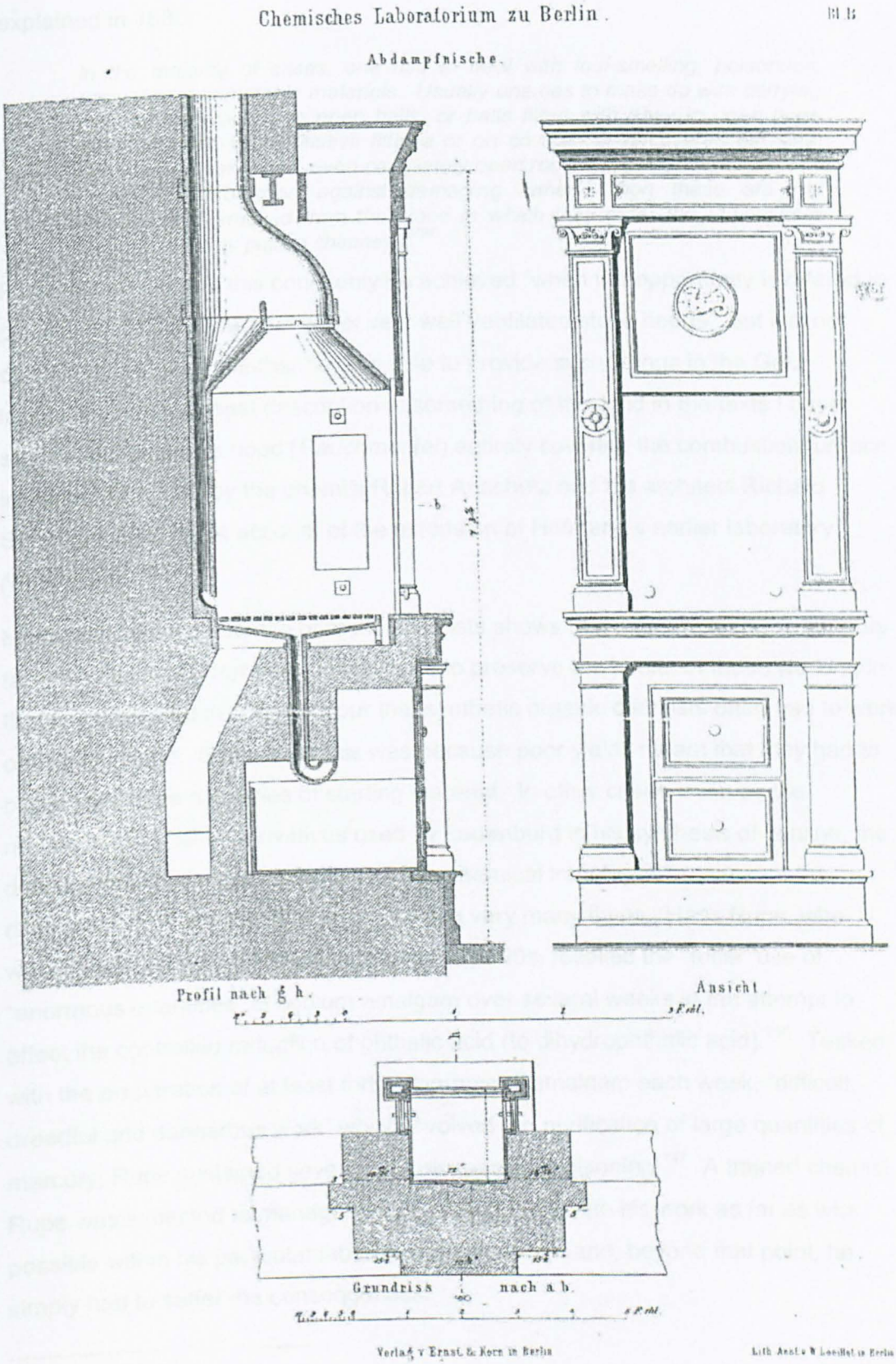


Figure 26. Hofmann's evaporation closets protected those working in the laboratory from damaging fumes. Cremer 1868, Blatt B.

explained in 1880:

> *In the majority of cases, one has to deal with foul-smelling, poisonous, corrosive or flammable materials. Usually one has to make do with carrying out such operations in open halls, or halls fitted with easy to open large windows, with very primitive fittings or on covered or uncovered terraces. But the best-ventilated, even completely open rooms, provide only extremely incomplete protection against damaging fumes, when these are not immediately removed from the place in which they enter the atmosphere through strongly pulling chimneys.*[794]

Pebal explained that this could only be achieved "when the opportunity is offered to place even large apparatus under very well ventilated stove hoods", but it is not clear from his book whether he was able to provide such fittings in the Graz laboratory. The earliest description of something of this kind in the texts I have studied is the smoke hood (*Rauchmantel*) entirely covering the combustion furnace in Bonn, described by the chemist Robert Anschütz and the architect Richard Schulze in their 1904 account of the extension of Hofmann's earlier laboratory (Figure 27).[795]

Meanwhile, the experience of many chemists shows that late-nineteenth laboratory facilities frequently remained inadequate to preserve the health of those working in them. I explained in Chapter Four that synthetic organic chemists often had to work on a large scale. Sometimes this was because poor yields meant that they had to begin from large quantities of starting material. In other cases, such as the reduction of pyridine derivatives used by Ladenburg in his synthesis of coniine, the difficulty of achieving apparently feasible chemical transformations meant that chemists had to attempt the same reaction very many times. Hans Rupe, who worked with Baeyer in München during the 1890s, recalled the "futile" use of "enormous quantities" of sodium amalgam over several weeks in the attempt to effect the controlled reduction of phthalic acid (to dihydrophthalic acid).[796] Tasked with the preparation of at least forty kilograms of amalgam each week, "difficult, dreadful and dangerous work" which involved the purification of large quantities of mercury, Rupe sustained severe, chronic mercury poisoning.[797] A trained chemist, Rupe was expected to manage the risks associated with his work as far as was possible within his particular laboratory environment and, beyond that point, he simply had to suffer the consequences.

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[794] Pebal (1880), 6.
[795] Anschütz and Schulze 1904, Abbildung 10, check page number. The major part of the extension involved adding a second storey to Hofmann's original building.
[796] Rupe 1932, 6-7. This work formed part of Baeyer's extended programme of research to establish the constitution of benzene by experiment.
[797] Ibid., 7.

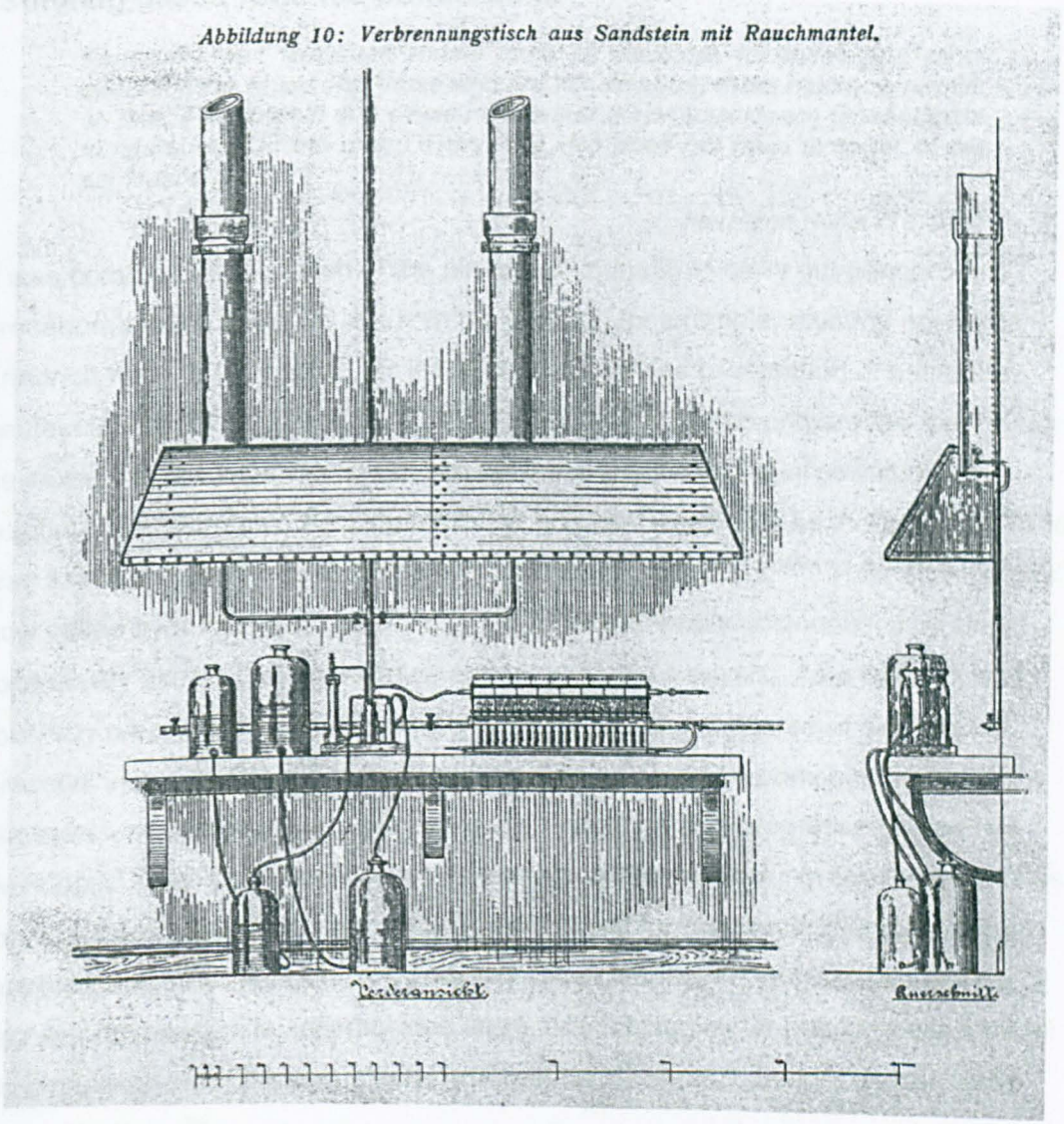


Figure 27. The smoke hood (*Rauchmantel*) covered larger assemblies of apparatus and prevented any fumes evolved from contaminating the laboratory atmosphere. Anschütz and Schulze 1904, Abbildung 10.

## "Stinking gases" and the Stinkzimmer[798]

> *Especially well ventilated rooms must be available for these and other operations in which only those who are actually busy there right now remain so that, if as a result of a single inadvertent act or coincidence unbreathable fumes spread in the room, everybody else does not have to suffer at the same time.*
>
> *Hermann Kolbe (1872)*[799]

It was common during much of the nineteenth century to carry out dangerous procedures in the open air. Early in the century, for example, a young apothecary Friedrich Kützing almost lost his life during an open-air preparation of antimony pentasulphide (*Goldschwefel*). In his hurry to complete the preparation before lunch, he mixed the reagents too quickly, causing the evolution of a large volume of sulphuretted hydrogen. Kützing fell to the ground "senseless, as though dead", and was saved only by the swift action of some nearby labourers.[800] This "stinking gas", now called hydrogen sulphide and known to be extremely poisonous, was also extensively used in both qualitative and quantitative analysis. As a result, it was routinely prepared and used by every student following a course of elementary practical instruction in chemistry, creating – as I mentioned earlier in the case of Giessen – serious laboratory air pollution. As the century progressed, chemists developed a variety of approaches to managing this problem. In some laboratories, including Kolbe's at Marburg, a balcony was used for the preparation of hydrogen sulphide and other dangerous gases including chlorine.[801] Hofmann's Berlin laboratory, meanwhile, incorporated large, central loggias for outside work, as well as a mains system through which hydrogen sulphide could be piped around the entire institute.[802]

As at Marburg, Kolbe's Leipzig laboratory had specially built balconies for performing dangerous operations and photochemical reactions.[803] Nevertheless, Kolbe still considered the pervasive smell of hydrogen sulphide throughout the institute to be "an as yet unsolved problem", and he proposed that the best solution was to confine the preparation and use of this gas to a single room.[804] Kolbe published his first description of this room and its dedicated apparatus for producing

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[798] Kolbe 1872, 442 ("übel riechenden Gasen"); Fischer and Guth 1901, 46 (*Stinkzimmer*).
[799] Ibid., XX.
[800] Friedrich (1995, 52) extracted from the memoirs of Friedrich Traugott Kützing.
[801] Kolbe 1865, 11.
[802] Hofmann 1866, 320.
[803] Kolbe 1872, XXVIII.
[804] Kolbe 1868, 19.

hydrogen sulphide (Figure 28) in 1871.[805] In addition to its health benefits, Kolbe justified his plan on pedagogical grounds. Whereas previously student practical exercises had been mainly confined to analysis, preparative organic chemistry now provided plentiful opportunities for students to acquire the skill in assembling apparatus that in the past they had learned from making hydrogen sulphide.[806]

Kolbe's innovation seems to have been extremely successful. When Festing inspected the outside working areas at Leipzig later that year, he found clear signs that they were no longer used: "judging from the fact that the water supply pipe was burst, apparently by the winter frost, this place does not seem to be much used".[807] Laboratories elsewhere quickly incorporated similar rooms. The special room in Leopold Pebal's 1880 Graz laboratory was directly modelled on Kolbe's (Figure 29).[808] Even Baeyer's München laboratory included a room for the preparation of hydrogen sulphide, although Baeyer generally opposed the provision of small rooms such as those for advanced students "in order to promote communication between those working in the laboratory".[809] Only Emil Erlenmeyer, Professor of chemistry at the Polytechnic in München, preferred to keep apparatus for preparing hydrogen sulphide in the main teaching laboratories, so that students would learn how to prepare it for themselves.[810]

Kolbe's approach continued to find favour well into the twentieth century. In Fischer's Berlin institute, for example, the use of hydrogen sulphide was confined to the *Stinkzimmer*. This extremely well ventilated room contained several fume cupboards and ice stores and was used for experiments involving hydrogen sulphide, as well as chlorine and ammonia which were stored in liquid form on a glass-roofed balcony outside the room.[811] Even though Robins reported that the somewhat earlier laboratory built for Lunge at the Zürich Polytechnic was thought to have done away with the need for a *Stinkzimmer* altogether by ensuring that "*all* rooms are adapted for carrying on all sorts of work without nuisance", the provision of special rooms for dangerous operations became and has remained routine.[812]

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[805] Kolbe (1871) reprinted in Kolbe (1872, 441-451). It included sections on ventilation, heating and the new apparatus for hydrogen sulphide, illustrated on p. 449.
[806] Kolbe 1865, 24-25.
[807] Festing 1871, 9.
[808] Pebal 1880, 20, and see also Tafel VI.
[809] Baeyer and Geul 1880, 4.
[810] Robins 1887, 52.
[811] Fischer und Guth 1901, 46.
[812] Robins (1887, 63) concluding an extensive description of the Zürich laboratory taken from *Industries*, issue 18, 29th October, 1886.

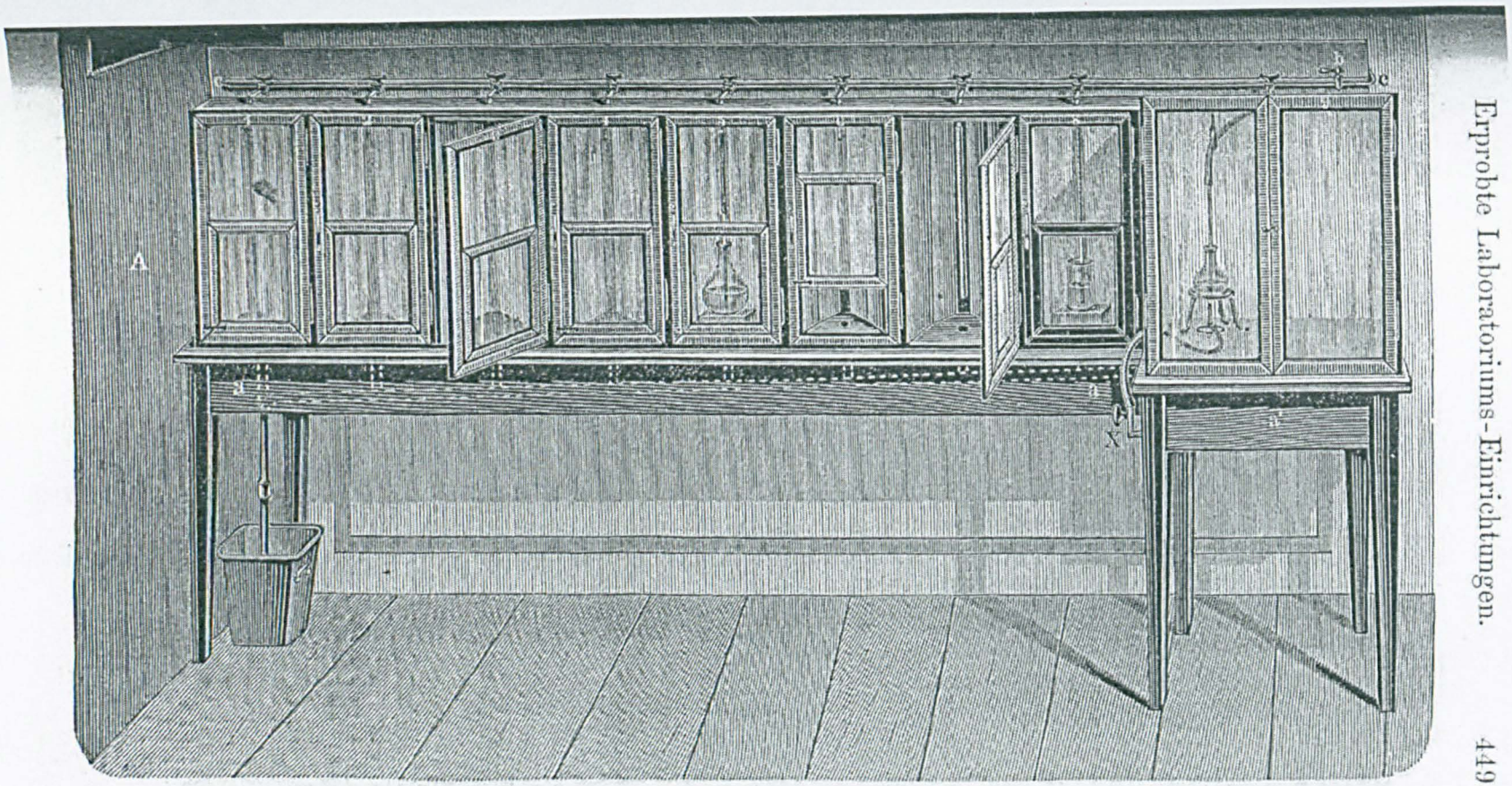


Figure 28. This dedicated apparatus for the production of the highly poisonous and widely used gas hydrogen sulphide occupied a special room in Kolbe's Leipzig laboratory. Kolbe 1872, 449.

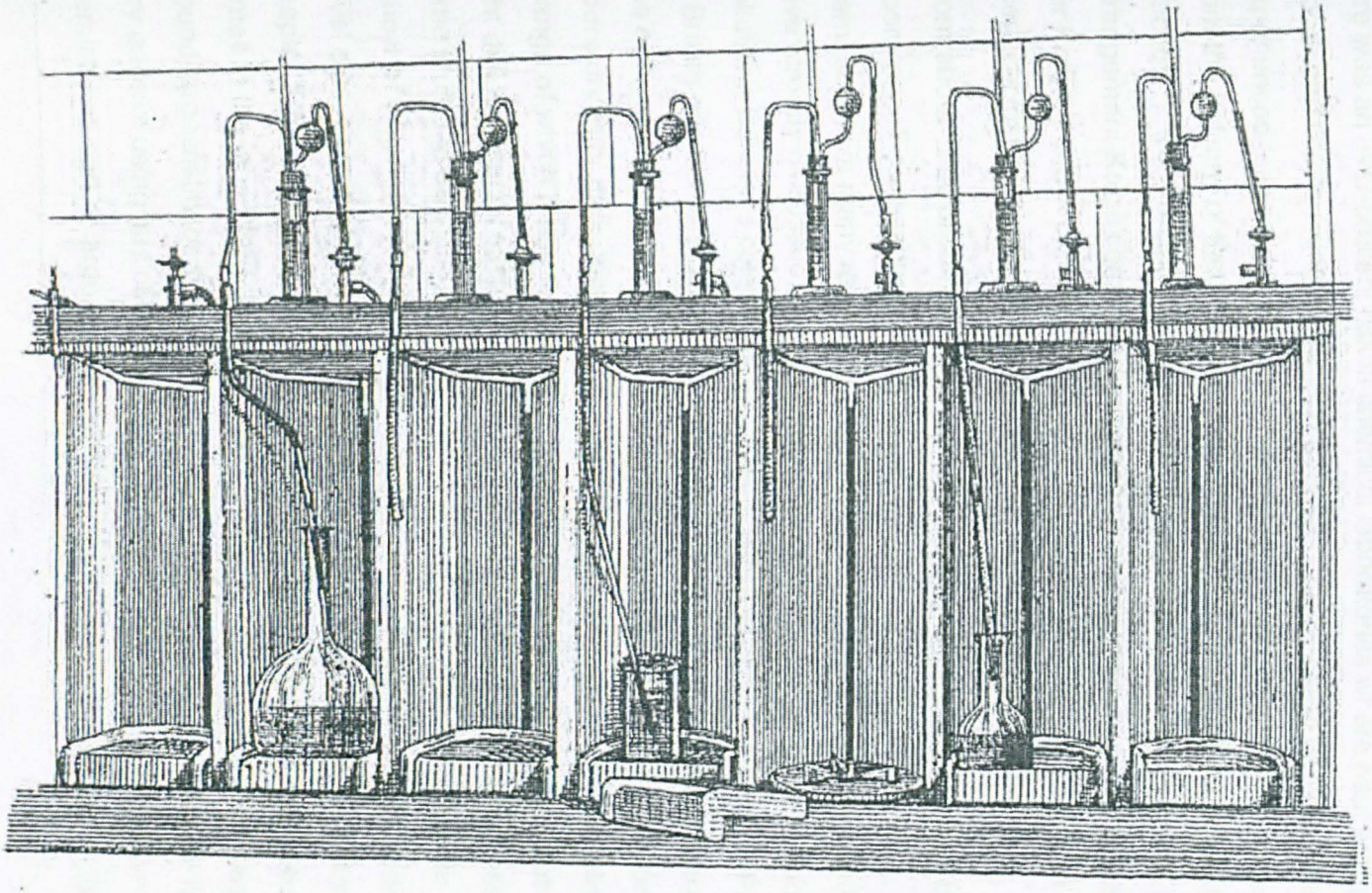

Figure 29. Kolbe's design was adopted by other chemists. This example is from Pebal's 1880 Graz laboratory. Pebal 1880, Tafel VI.

## Preventing a Conflagration

> *The coincidental circumstance, that I used for a long time to live opposite the laboratory in Marburg, enabled me twice to discover outbreaks of fire in the laboratory so early that it was possible to prevent a conflagration.*
>
> *Hermann Kolbe (1868)*[813]

Fire was an ever-present risk in chemical laboratories where heat was provided by wood- and coal-burning stoves and furnaces. Kolbe learnt from his Marburg experiences (see epigraph), ensuring that the new Leipzig laboratory was visible from the balcony of the study in his residence.[814] In accordance with standard practice,[815] the director's residence at Leipzig was in the main institute building, an arrangement Kolbe considered substantially reduced the strain of his situation.[816] For Kolbe, the risk of fire in a chemical laboratory was so great that the director of a chemical institute was never off-duty.

From about 1860 onwards, two factors combined to transform the risk of fire in the laboratory. First was the increasing use of gas for heating and lighting, which had a dramatic and in many respects positive effect on the laboratory environment. As I have already discussed, the use of gas rather than coke as a fuel reduced air pollution. Bunsen's celebrated adaptation, with the instrument maker Peter Desaga, of British gas burners during the mid-1850s provided the chemistry laboratory with one of its most enduring icons.[817] Gas lighting enabled chemists to work in the laboratory after dark, thereby substantially increasing their winter working hours – a change of which Kolbe for one approved.[818] For the first time, it was possible to light difficult spaces such as lecture theatres adequately for evening use.[819] At the same time, the handling and preparation of a growing variety of organic substances – most of which were highly flammable and many of which were explosive – using novel glassware-based techniques for purification and reaction (discussed in Chapter Four) substantially increased the risks associated with the use of open flames in the laboratory. New infrastructure by means of which gas was piped around large institutes provided chemists with instantaneous heat and light, but the very ease of using gas combined with the introduction of preparative organic chemistry as part of large-scale laboratory training increased both the likelihood of

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[813] Kolbe 1868, fn. 27.
[814] Kolbe 1868, 26-27.
[815] Kolbe 1865, 12.
[816] Kolbe 1868, 26-7; and direct quotation from footnote on p.27.
[817] See Roscoe (1906, 51-2) on Bunsen's development of his eponymous burner.
[818] Kolbe 1865, 11.
[819] Kolbe (1872, XXXII-XXXIII) described the large auditorium which was illuminated during evening lectures by "a hundred flames".

fire and its potential consequences. Not only were relatively inexperienced chemists now routinely handling inflammable organic substances in fragile glass flasks, but they were often doing so in large, open laboratories where even a small fire could soon lead to catastrophic consequences.

Gas was also an expensive consumable resource, so that it was desirable to minimise its waste. According to Pebal, the escaping gas from a single open gas tap was so effectively removed by the ventilation system in Graz that it could pass unnoticed for an entire year. With over 700 gas taps throughout the institute, moreover, it was quite impossible to check every tap every evening. Pebal solved this problem by implementing the system developed in the laboratory at Pesth, where intermediate valves allowed the gas supply to various parts of the institute to be shut off and a manometer made it possible to check for leaking gas. The only modification Pebal made at Graz was to include a master gas tap for the entire institute, a system he commended for domestic as well as laboratory use.[820]

By the turn of the century large institutional laboratories were well provided with hydrants, hoses and other fire equipment. In Bonn, for example, there were four large and fourteen small hydrants on corridors throughout the building. A cupboard in the basement contained fire equipment and a hose was located in the entrance lobby of the room for organic combustions (Figure 30).[821] In 1901, Fischer's Berlin institute was constructed with six hydrants in the grounds. There were seven fire hoses and numerous spray pipes (*Strahlrohren*) throughout the building. Showers (*Wasserbrausen*) had been installed in all the laboratories to extinguish burning clothes, and posters showing the location of all these items were in the entrance hall to each floor. The fire alarm was directly under the control of the Berlin fire department.[822]

These material approaches to fire prevention and management went hand-in-hand with practice-based methods of minimising the risk of fire, explosion and other laboratory accidents. In 1887 Fischer published his *Introduction to the Preparation of Organic Compounds*, the first book designed to accompany a practical course in preparative organic chemistry. By 1905, in the seventh German edition of his book, Fischer explained that: "In order to prevent accidents, the students in this laboratory

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[820] The master tap did not shut off the supply to the director's laboratory nor the rooms for prolonged operations. See Pebal 1880, 16.
[821] Anschütz und Schulze 1904, 16.
[822] Fischer und Guth 1901, 16.

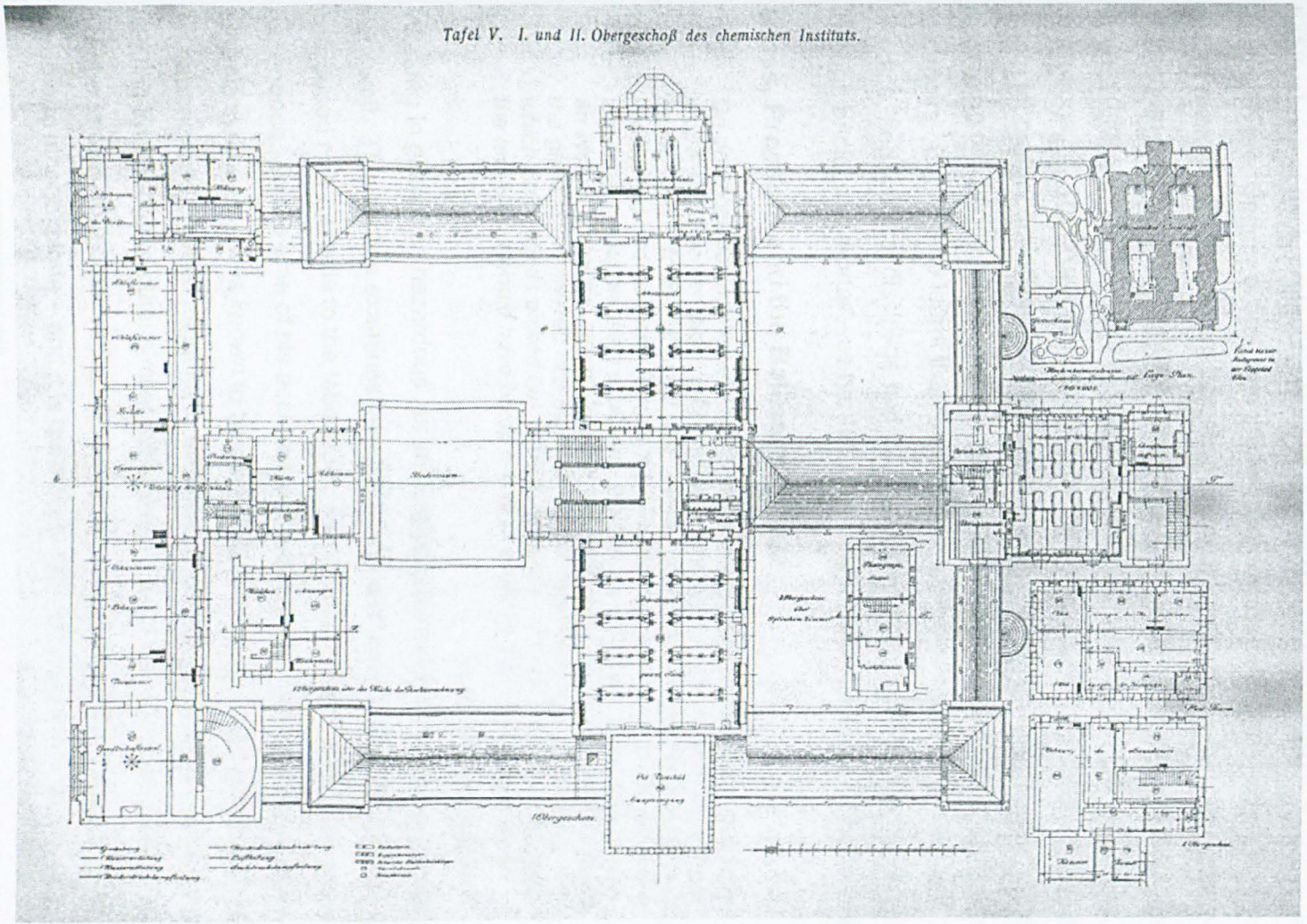


Figure 30. Anschütz's remodelled Bonn institute was well equipped with fire hydrants and a fire hose (*Brause*).

are made aware of the dangers of chemical work by means of detailed notices, and it seemed to me advisable to place these warnings at the beginning of this book."[823] Fischer's "Precautions necessary for the avoidance of accidents" began by warning students that: "As the eyes are more especially endangered in chemical work, the habitual use of thick, protecting glasses is urgently recommended." The first section dealt with the "Danger of fire", and the longest devoted well over two pages to the risk of explosions. Fischer singled out the use of sealed tubes and the performance of vacuum distillations as particularly hazardous in this regard, and he emphasised the need for student chemists to wear eye protection whilst carrying out these operations.[824] The experience of teaching synthetic organic chemistry in Hofmann's Berlin laboratory during the last decade of the nineteenth century taught Fischer that managing risk had to be instilled through laboratory training and enshrined within textbooks. But he also learnt that, as with so many other aspects of chemical practice, pedagogical discipline had to be supplemented by discipline imposed through bricks and mortar – as his 1901 Berlin laboratory so richly demonstrated.

## Glass, Pressure and the Ballistic Cabinet

> *On one occasion, however, I had been working on perchloric acid, and I had prepared some perchloric ether, which I was anxious to analyse, as this had never been done. It was well known to be an excessively explosive substance, and as I was filtering a few cubic centimetres of the liquid into a test-tube, the whole thing exploded, the bottom of the test-tube bored a hole, an inch in diameter, almost through the hard wood of the filter-stand, whilst the glass was shivered into many thousand fragments in my left hand, from which I afterwards picked out some 200 pieces. If I had had my hand under the test-tube it would have bored a hole in it just as it did in the filter-stand.*
>
> *Henry Roscoe (1906)*[825]

Working in glass was hazardous, as the English chemist Henry Roscoe understood very well. This section examines how the practice of synthetic organic chemistry introduced new hazards to the laboratory, one of which is indicated by Roscoe's experience. By the time of his accident, perchloric ether – an artificial product of organic synthesis – was *known* to be potentially explosive. *How* was this known? An experienced chemist might have anticipated such behaviour by comparison with existing knowledge of other similar substances, but in the end such a thing could only be known from observation. So someone, somewhere had already seen perchloric ether explode – and it is quite likely that the experience was a very

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[823] Fischer (1909, vii-ix) reprinted the Preface to the 7th German edition. The direct quotation is from p. viii.
[824] Fischer 1909, xi-xvi.
[825] Roscoe 1906, 108. Roscoe, who had trained with Robert Bunsen, became first Professor of Chemistry at Owens College in Manchester.

considerable shock. When chemists prepared new substances, they could only predict – and never be certain – what their properties would be. Would they be explosive or inert, sweet- or foul-smelling, curative or poisonous?

During the 1840s, chemists often heated substances in sealed glass tubes in the attempt to produce chemical transformations.[826] This method made it possible to heat substances to temperatures well in excess of the boiling point of the mixture of reactants and under extremely high pressure but the combination of high pressure and temperature within glass proved to be extremely hazardous, as did the entirely unpredictable behaviour of the new substances created. The English chemist Edward Frankland made extensive use of sealed tubes during his investigation of the organic radicals during the late 1840s, developing the technique so as to remove all traces of air before sealing and heating the tubes.[827] Frankland's experiences higlight the risks associated with forming new substances. In one accident during a visit to Bunsen's laboratory at Marburg in the summer of 1849, he suffered zinc poisoning whilst investigating the residue a reaction in a recently opened sealed tube:

> *On pouring a few drops of water upon this residue, a greenish-blue flame several feet long shot out of the tube, causing great excitement amongst those present. Professor Bunsen, who had suffered arsenical poisoning during his researches on cacodyls, suggested that the spontaneously inflammable body, which diffused an abominable odour throughout the laboratory, was that terrible compound, which might have been formed by arsenic present as an impurity in the zinc used in the reaction, and that I might be already irrecoverably poisoned. These forebodings were, however, quelled in a few minutes by an examination of the black stain left upon porcelain by the flame; nevertheless I did afterwards experiences some symptoms of zinc poisoning.*[828]

Frankland's phlegmatic description of what was surely an alarming incident draws our attention to a crucial difference between chemical practice in research and pedagogical contexts. Frankland was an experienced chemist, an expert manipulator and, crucially for the safety of this procedure, a highly skilled glassblower. Frankland's experience shows that the use of sealed tubes was hazardous, even in the hands of its most experienced practitioner – and it suggests that, like Rupe, Frankland accepted this inherent risk.

Hofmann also made extensive use of sealed tube reactions whilst investigating organic amines and phosphorus bases in the laboratory at the RCC.[829] By the time

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[826] See, for example, Blyth and Hofmann 1843, 16.
[827] Frankland 1850, 265.
[828] Frankland 1877, 144-145.
[829] See, for example, Hofmann 1858, 9; and 1861, 291.

he returned to Germany from London a decade later, Hofmann was committed to the use of this method, which became a staple of the chemical practice taught in his Berlin laboratory. It was one of the main experimental methods by which chemists developed their knowledge and understanding of constitution and reactivity and it remained an important tool of synthetic organic chemistry until at least the end of the nineteenth century, also playing an important part in Ladenburg's synthesis of coniine (discussed in Chapter Four).[830]

Extending the use of sealed tubes nevertheless presented some serious practical problems. It was all very well for such skilled chemists as Hofmann and Frankland to accept the risks associated with this technique. By virtue of their training and experience, they were well equipped to assess and minimise those risks and to take vital decisions about what they should, or should not, attempt. As Fischer discovered, placing such a technique in the hands of relatively junior chemists meant that the risks inherent in the combination of high temperature and pressure, glass and dangerous chemicals had to be managed in other ways. Inexperienced chemists could not reliably be expected to perform such operations with the same skill as their vastly more experienced teachers, and the potential consequences of something going wrong were enormously magnified in large laboratories where dozens of chemists were at work.

As with the use of hydrogen sulphide discussed earlier, chemists implemented a variety of measures designed to manage the risks associated with using sealed tubes and to make the technique conform to acceptable standards of safety within the pedagogical environment. By the end of the century, as I have already mentioned, Fischer insisted on the routine wearing of safety glasses or goggles in order to prevent eye injuries following the explosion of sealed tubes and vacuum distillation apparatus. In the 1860s, before these procedures had become part of large-scale training, chemists had already taken steps to design the laboratory building so as to minimise the likelihood of injury. In Bonn, for example, Hofmann included "specially arched niches, let into the walls and provided with enclosing iron doors, for the protection of the manipulator when experimenting with substances at high temperature in sealed tubes".[831] In Leipzig, Kolbe described the provision of a room which was reserved for heating sealed tubes in baths containing paraffin oil.

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[830] Fischer (1909, 153 and 158) referred the use of sealed tubes in the preparation of α-methyl glucoside and racemic phenylalanine respectively.
[831] Robins 1887, 49. Note that, according to Festing (1871, 7) the outdoor spaces in Bonn were also equipped with a "strong iron box for containing tubes, in which substances can be heated if there is danger of explosion".

He explained that the room was "so arranged, that the glass debris that was hurled out by frequently occurring explosions collided with the stone walls and that the strongly pulling steam extractors, under which such a paraffin bath stood, quickly swallowed up the evolving fumes".[832] Baeyer's München laboratory also contained a dedicated room for heating sealed tubes referred to, appropriately enough, as the "cannon room". The room contained six air baths intended for heating sealed tubes, and behind each was a special wooden box designed to prevent glass fragments from flying around during explosions.[833]

Described in Anschütz and Schulze's 1904 book on the newly extended Bonn laboratory (Figure 31), the ballistic cabinet (*Schießschrank*) combined these three risk management strategies, providing protection against metal fragments from exploding bomb ovens (*Bombenöfen*) as well as against the glass debris produced by exploding sealed tubes (high pressure) and vacuum distillation apparatus (low pressure). Ballistic cabinets were located in three rooms of the Bonn laboratory. One, with space for simultaneous heating of ten sealed tubes – a way of scaling up synthetic procedures, as Ladenburg had done in his preparation of ethyl piperidine (see Chapter Four) – was in the basement. Another larger cabinet on the ground floor was intended for bomb ovens. It was divided into three compartments, each of which was closed by double doors made of wide-gauge strong wire mesh. The dividing walls were heavy, mobile hanging steel plates, designed to absorb the impact of flying metal.[834] On the first floor, a small room adjacent to the room for combustion analysis contained a ballistic cabinet with two compartments for the reception of bomb ovens. The room itself was accessed through a heavy iron door and the doors of the cabinet were massive and extremely strong. It was possible to see into the cabinet through slits in the doors that were closed with small mica plates. The cabinet could also be used for distillation of easily decomposable compounds under atmospheric or reduced pressure. As in the large cabinet on the ground floor, a mobile, heavy iron plate was used to divide the cabinet into two compartments and similar plates lined its fixed side walls.[835]

The *Schießschrank* encapsulates many of the features of laboratory design and construction dealt with in this chapter. It occupies the boundary between building

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[832] Kolbe (1872), XXIX.
[833] Baeyer and Guel 1880, 8; Robins 1887, 52.
[834] Anschütz and Schulze 1904, 39.
[835] Ibid. The illustration on p 40 shows a vacuum distillation apparatus set up inside the ballistic cabinet.

*Abbildung 23: Neuer Schießschrank R. Nr. 346, Seite 39.*

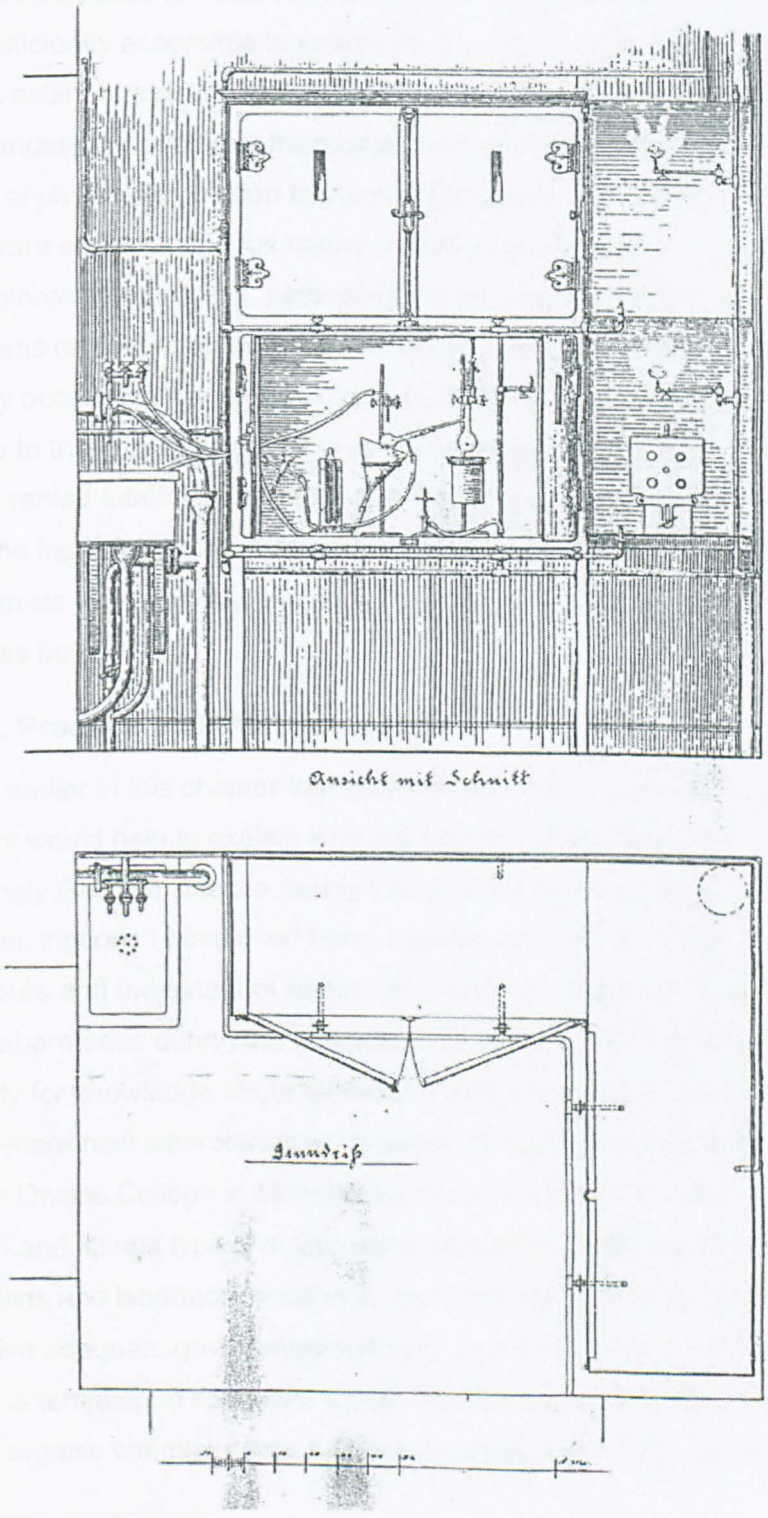


Figure 31. The ballistic cabinet protected chemists from the dangers associated with performing chemical operations within glass at extremes of temperature and pressure. Frequently used to contain sealed tube reactions, here a reduced pressure distillation apparatus is shown inside a ballistic cabinet in Anschütz' Bonn laboratory. Anschütz and Schulze 1904, Abbildung 23.

and equipment, the grey area between the responsibility of the chemist and the architect. Designing the ballistic cabinet drew on the experience and skill of the chemist, but incorporating it into the fabric of the building whilst at the same time making it sufficiently accessible to ensure its use was a challenge to the architect. The ballistic cabinet helped to maintain the safety of the institute as a whole, both by removing dangerous operations from large, communal laboratories and by providing a high level of physical protection to the practising chemist. Its existence made chemists aware of the hazardous nature of certain aspects of their work and it helped to enforce safe practice, particularly for inexperienced students. Installations like the ballistic cabinet enabled large numbers of young chemists to work at levels of purity only accessible by using vacuum distillation, and made it possible for them to contribute to the growing stock of preparative knowledge built by performing reactions in sealed tubes. I contend that without the ballistic cabinet and, by extension, the institutional laboratory as a whole, it would not have been possible for organic chemists to amass the "huge experimental material" upon which organic synthesis was built.[836]

## Pedagogy, Practice and the Laboratory

I suggested earlier in this chapter that understanding the laboratory as *part* of the chemistry set would help to explain why organic chemistry became such an overwhelmingly German science during the late-nineteenth century. The published laboratory descriptions I have used here, together with numerous laboratory inspection tours and the extent of academic chemists' movement between German and British laboratories during the nineteenth century, indicate that there was plenty of opportunity for knowledge about laboratory design and construction to reach Britain.[837] Where new laboratories were built in Britain, for example Roscoe's laboratory at Owens College in Manchester, they incorporated many aspects of the arrangement and fittings typical of German laboratories of the period.[838] What British chemists and laboratory architects could *not* recreate, largely because they did not receive adequate government funding, was the German laboratory as a whole and it is tempting to speculate that the British focus on largely theoretical questions in organic chemistry was a direct consequence of this deficiency.[839]

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[836] Elbs 1889, 1.
[837] The same is true of the French case, where the development of chemical laboratories during the nineteenth century has been discussed by Rocke (2001).
[838] Roscoe 1881. The architect was Alfred Waterhouse. The general accuracy of this comment is supported by Robins (1887, 113).
[839] See Nye (1994) on the London and Manchester schools of theoretical organic chemistry.

Whatever their training and interests, British chemists were simply not equipped to practise synthetic organic chemistry because they lacked an essential tool of disciplinary management – the laboratory.[840]

Some evidence for this speculation is available from the variety of German texts written to accompany the new practical courses in organic synthesis, several of which have already been mentioned at various points throughout this dissertation. These books – including Fischer's 1887 *Introduction to the Preparation of Organic Compounds*, the compendia of synthetic methods published by Elbs and Lellmann in the late 1880s, and Ludwig Gattermann's 1894 laboratory manual *The Practice of the Organic Chemist* – were all written by young chemists then teaching practical courses in synthetic organic chemistry at German universities, and they provided an essential practical complement to established textbooks of organic chemistry.[841] Together these books formed the canon of late-nineteenth century organic synthesis and, although English language editions of Fischer's *Introduction* and Gattermann's *Practice* appeared in 1889 and 1896 respectively, neither Elbs' nor Lellmann's book was ever translated into English. Furthermore, although Fischer's book had some influence on British organic chemistry, the translation of Gattermann was primarily intended for an American audience.[842] Other British books, most notably Julius Cohen's 1892 *The Owens College Course of Practical Organic Chemistry*, owed a considerable debt to Fischer's work. Owens College was the British institution most closely modelled on German chemical laboratories of the period, and its professors of chemistry Roscoe and Schorlemmer considered Cohen's first book to fill "a lacuna in our English chemical literature".[843] Nevertheless, its extremely limited scope compared with Fischer's *Introduction* serves to reinforce my claim that synthetic organic chemistry was not being taught or practised to any significant extent in Britain during the late-nineteenth century.

One particular aspect of the practice of synthetic organic chemistry as I have described it provides further confirmation of this idea. Throughout this dissertation I have emphasised the importance of glass and glassblowing to the development of

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[840] William Perkin, Jr. is a notable exception to this. Morrell (1993, 108-110 and 118-119) described the new laboratories at Manchester and Oxford in which Perkin pursued the synthesis of organic compounds.
[841] Fischer's book was conceived during his time at Erlangen and published whilst he was Professor of Chemistry at Würzburg. Lellmann was a *Privatdozent* at Tübingen, whilst Elbs and Gattermann were *ausserordentliche Professoren* at Freiburg and Heidelberg respectively. Kekulé 1859-1866 and Gerhardt 1853 were established mid-century textbooks.
[842] The first and many subsequent editions of Gattermann in English were published in New York.
[843] Cohen 1892, "Preface".

organic chemistry, and particularly synthetic organic chemistry, during the nineteenth century. I argued in Chapter Four that these uses of glass came increasingly to depend on the existence of specialist chemical glassblowers such as Geissler, who were able to translate chemists' glassware innovations into standard, commercial items. In Bonn, the home of Geissler's glassblowing firm, glassblowing facilities were provided in the operations room attached to each of the main teaching laboratories. According to Hofmann, these blowpipe-tables were "scarcely ever at rest". Institutes elsewhere – for example Baeyer's in München – included a dedicated room for glass blowing.[844] In these German laboratories, glassblowing was an everyday part of chemical practice, learnt by chemists from very early in their training.

In Britain, by contrast, access to glassblowing skill had not changed much in over half-a-century. When the chemistry teacher William Shenstone published his *Methods of Glassblowing* in 1886, he explained that:

> *The opportunities of obtaining practical instruction in the art of glass-working are so few in this country, and the advantages to be derived from an acquaintance with that art are so considerable to those who are engaged in physical and chemical experiment, that it appears to me a treatise on the subject is likely to be useful.*[845]

Shenstone's book, which appeared in a second enlarged edition in 1889, was the first of a new wave of glassblowing manuals published during the decades either side of 1900. But unlike the books published during the 1830s (discussed in Chapter Four) only one of these, written by the physicist Hermann Ebert, was intended for a German audience. Ebert's book, moreover, was predominantly concerned with physics – including the recent discovery of X-rays by Wilhelm Conrad Röntgen – and had little to say about chemical apparatus, even though it drew heavily on Shenstone's text.[846] Other books in this group, including those by Francis Frary in Minnesota and Djakonow and Lermantoff in St. Petersburg, dealt with basic chemical glassblowing and I suggest that, like Shenstone, these authors were attempting to make glassblowing skill available to chemists in their surroundings.[847] Chemists in Britain, the United States and St. Petersburg in the late-nineteenth and early-twentieth centuries, unlike their German counterparts, did not learn chemical glassblowing as part of their hands-on laboratory training, and I

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[844] Hofmann 1866, 301; Baeyer and Geul 1880, 8.
[845] Shenstone 1886, v.
[846] Ebert (1904, iv) included X-rays amongst his reasons for updating the previous 1895 edition.
[847] Frary 1914; Djakonow and Lermantoff 1895.

propose that they were largely prevented from contributing to the development of synthetic organic chemistry as a result.

The preceding sub-sections have shown how institutional laboratories both reflected and were used to manage aspects of late-nineteenth century chemical pedagogy and practice, and they combine to produce a powerful vision of these laboratories as essential tools of chemical work and training. According to the chemists whose work I have used in this study, the design and construction of the laboratory was every bit as vital to the disciplinary development of chemistry as any piece of apparatus, any experimental technique or, indeed, any theory. This recognition expands our notion of what constitutes the material culture of chemistry to include the laboratory building as well as the test-tube. It also demands that we take the location of production of chemical knowledge seriously – and I propose that by so doing we will move beyond understanding the laboratory as merely a "place of knowledge".[848]

It is more than twenty years since Owen Hannaway argued that both social and technical considerations influenced the design of chemical laboratories around 1600 but this chapter shows that such a claim, though certainly applicable to the nineteenth-century laboratories studied here, is nevertheless too weak.[849] Hannaway emphasised "the importance and distinctiveness of the places within" the Chemical House of Andreas Libavius, as a result of which he perceived the laboratory as an expression of what he called the "active" mode of scientific life, an architectural manifestation of social and political ideals.[850] Perhaps because of his focus on the activity of the scientist, I contend that Hannaway relegated the laboratory to an overly passive role when he described it as "the common place that housed the particular places of chemistry."[851] To chemists like Hofmann and Kolbe, as this chapter has illustrated, a chemical laboratory did much more than merely *house* a complicated array of rooms devoted to the specific activities which produced scientific knowledge: the laboratory was *instrumental* in producing that knowledge.[852]

In 1988 Steven Shapin hoped to encourage historians of science to study the sites of knowledge production because those places "counted as a partial answer to the

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[848] Ophir and Shapin 1991, 3.
[849] Hannaway 1986, 599.
[850] Ibid., 608.
[851] Ibid., 609.
[852] Hofmann 1866, 299; and see my earlier comments about Kolbe's (1865 and 1872) integration of laboratory description, training and published output.

fundamental question, Why ought one to give one's assent to experimental knowledge claims?"[853] Shapin made a powerful case for the importance of social structures in determining the course of scientific activity, and he was at least partly successful in persuading historians of the need to consider *where* science was being done, *to what end* and *by whom*.[854] I have shown that in the case of late-nineteenth century organic chemistry the laboratory was essential to the material production as well as the validation of new knowledge, transcending the distinction between the technical and the social. The institutional laboratory performed vital functions in experimental organic chemistry. Some of these functions might be considered social – for example, the organisation of the learning and research community in accordance with best pedagogical practice – but others, including the management of risks so severe they could no longer be left in the hands of the individual, are undeniably technical. The exterior facades of Germany's magnificent palaces of chemistry certainly laid claim to a superior position in the social and cultural landscape but I have shown that considerations of practice and pedagogy were essential in shaping the laboratory's interior layout and fittings, without which there would have been no knowledge to warrant and no discourse to police.[855]

## Conclusion

I have focused throughout this dissertation on the practice of chemistry, a powerful approach which has transformed the historical material I have examined. Above all, it has restored a sense of what I shall call *historical inertia* to the history of nineteenth-century organic chemistry, showing why organic chemistry developed in the places and at the pace it did. In the case of organic analysis, for example, I have argued that Liebig's decision to focus on the alkaloids was largely prompted by professional rivalry, and that both personal circumstances and geographical situation significantly affected his approach to the technical difficulties encountered in the course of that work. My work has also undermined the notion that Liebig's introduction of the *Kaliapparat* instantaneously reduced quantitative analysis to a routine manipulative task whose results could be converted into formulae by a straightforwardly deductive arithmetical process. So, although the roughly three months during which Liebig developed the *Kaliapparat* are a legitimate focus of historical interest, concentrating on this period at the expense of the several years on either side has tended to obscure the motives for and difficulties associated with

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[853] Shapin 1988, 274.
[854] Meinel 2000 is an especially relevant example of this response.
[855] Shapin 1988, 273-274.

Liebig's work in the area of organic analysis. Following Liebig as he first realised the ambition and acquired the skills to tackle the analysis of the alkaloids and then, with the help of his students and assistants, stabilised his new method of analysis, on the other hand, has illuminated the processes by which Liebig transformed both organic analysis and chemical pedagogy, and by which he was himself transformed.

The method of organic analysis developed and taught by Liebig in Giessen involved work, training and – as I mentioned earlier in this chapter – the material facilities of a new, communal laboratory. The same concept applied to organic synthesis has equally far-reaching consequences. Once we recognise the immense work involved in developing and propagating the new practice of organic synthesis, with its attendant problems of chemical identity and transformation, we can no longer accept that the artificial production of natural substances such as quinine was as insignificant – theoretically and otherwise – to the development of chemistry as most histories would like us to be believe. Chemists in the mid-nineteenth century may have vastly underestimated quite how much work it would take to achieve the synthesis of quinine but they laboured for more than a century to achieve this goal, raising magnificent palaces for the new discipline of synthetic organic chemistry in the process.

What did these chemists hope to achieve? I explained in Chapter Three that the artificial production of quinine was potentially extremely lucrative. It was also a medically and scientifically important goal, which I propose was heavily related to late-nineteenth century organic chemists' approach to their own history. Organic chemists repeatedly and publicly promoted both the utility and the scientific credentials of their discipline – as, for example, in the lectures I have already mentioned delivered by Hofmann (*Organic Chemistry and the Teaching of Medicine*) and Baeyer (*On Chemical Synthesis*) during the 1870s.[856] At the same time, these chemists were involved in a serious struggle in the laboratory, where the increasingly hazardous nature of experimental organic chemistry was threatening its conformity to the academic environment.

Chemists had not found it easy to gain admission to the university for their laboratories. In early-eighteenth century Leipzig, for example, the first professor of chemistry's petition for a laboratory was refused on the grounds that it would be used to prepare "not only arsenical compounds (*Arsenicalia*), which are themselves

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[856] Compare, for example, Hofmann's (1871b, 10) use of quinine to raise the status of organic chemistry with Baeyer's (1878, 4) appeal to the scientific credentials of synthetic organic chemistry.

nothing other than the strongest poison, but also antimony compounds (*Antimonalia*) and ammonia (*Spiritus Urinosi*), which cause a terrible stink".[857] A chemical laboratory was an unwelcome addition to the university not only because it represented the introduction of manual labour better kept in the workshop. It was also too dangerous, threatening to make the environment unbearable to scholars in the vicinity. Yet only a place within the university could elevate chemistry from its position as an auxiliary to medicine to the status of an independent science, an achievement to some extent confirmed within reformed German universities by chemistry's move from the medical to the philosophical faculty during the early-nineteenth century.[858]

Towards the end of the nineteenth century the notion of a science was increasingly related to ideas of discipline and training, and I contend that this is the context in which we should view the risks of fire and explosion, injury and poisoning which accompanied the development of synthetic organic chemistry. Organic chemists had to work hard during the late-nineteenth century to maintain the academic credentials of their discipline, and the laboratory was fundamentally implicated in this effort. Only an entirely new kind of laboratory, chemists learned, could contain the risks of large-scale training and research in organic synthesis within limits acceptable to students, their parents and, crucially, university administrators. Purpose-built laboratories were essential to the *scientific* practice of organic synthesis but – as I discuss in more detail below – their construction also changed perceptions of what *defined* a science.

For Liebig, Hofmann and Ladenburg and their peers, chemists' knowledge resided in their hands just as much as their heads, a combination Kolbe neatly encapsulated in the term "thinking chemically" – by which he meant the ability "to handle chemical questions skilfully, to remove encountered difficulties by the simplest means, and to draw correct conclusions from the results obtained" and which he regarded as "the secret of the famous Giessen school".[859] Practice in the laboratory was essential to developing chemical skill, something Kolbe likened to learning to swim, or to speak a new language.[860] It is, perhaps, no coincidence that we owe the identification of tacit knowledge as underlying "every single act of articulate communication" to the

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[857] Hantzsch 1909, 70.
[858] Meinel 1988, 104.
[859] Kolbe 1865, 27.
[860] Kolbe 1872, XXXVI-XXXVII.

*chemist* and philosopher Michael Polanyi.[861] Theory and practice might be partially separable in pedagogical settings – as reflected in the division between the largely theoretical content of textbooks and the practical emphasis of laboratory handbooks. Nevertheless, as the examples in this dissertation show, chemists' production of new knowledge depended on integrating the two, comparing many candidate experimental outcomes with the possible consequences of their theoretical convictions.

In Giessen, Liebig and his students compared the numerical results of quantitative analysis with formulae whose theoretical plausibility they judged by reference to a wide range of additional experimental data. Fifty years later, Ladenburg prepared numerous substances in the hope that one of them might prove to be coniine. Ladenburg's key criterion of identity was melting point, whose comparability was only maintained through meticulous and highly standardised practice. Theory certainly guided Ladenburg in what to make, and the substances he produced refined his theories, but this loop could not be closed until Ladenburg made the *one* substance whose physical and chemical properties convinced him and his peers that it was identical to the natural base. Chemists' daily work depended on trial and error, minimising uncertainty and selecting provisional solutions which were *most plausible* in relation to the current state of both theory *and* experimental knowledge.

These negotiated, provisional solutions were highly located in physical as well as social terms. Giessen analysis, for example, was not just the product of Liebig's particular approach to the performance of manipulative techniques and the interpretation of the resulting numerical data – what I have called his *philosophy of practice*. It was also produced by organised labour within a new kind of communal laboratory setting. I have argued that Liebig found it difficult to spread this highly skilled philosophy of practice beyond his Giessen laboratory. The present study has not addressed this question explicitly, but it seems reasonable to speculate that when Giessen-trained chemists moved to new locations, they were frequently unable to continue to practise organic analysis in the way they had learnt from Liebig because they lacked essential aspects of the Giessen laboratory setting. There is only one well-studied example where the Giessen approach to organic analysis was successfully relocated in its entirety: Hofmann's new laboratory at the RCC in London.

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[861] Polanyi 1962, 203; and see also Ravetz (1971, Chapter 3) on "science as craft".

There is nothing new in the idea that training and laboratories are essential components of the mechanism by which knowledge can be made to travel.[862] Nevertheless, understanding the extent of the required integration between knowledge production, training and the laboratory space in the case of organic chemistry has important consequences. For one thing, it underlines the inseparability of training and research, and it situates what Fischer termed "the intimate, old German connection between research and teaching" firmly within the four walls of the laboratory.[863] In doing so, it suggests a potentially fruitful merger between historical studies of chemical pedagogy and of the laboratory. In this dissertation, for instance, although I have related the research practices of Liebig, Hofmann, Schotten and Schiff to their training, I have made few explicit references to the laboratory setting of their work until this last chapter. In the significant case of Ladenburg, furthermore, I have said much about research but almost nothing about training.

The two final chapters of this dissertation suggested two historical discontinuities separated by about fifteen years: one in the 1880s between the research practice of Hofmann and Ladenburg; the other in the late 1860s between laboratories created in existing buildings and those that were purpose-built to incorporate chemists' design requirements. Given what I have said about the connection between laboratories and chemical practice, it would be reasonable to seek at least a partial cause of the first discontinuity of practice in the second, earlier discontinuity in laboratory design and construction. Much more research into the relationship between training, research practices and the laboratory environment of synthetic organic chemists including Baeyer and Fischer would be essential to test this connection, but Ladenburg's career provides some positive initial indications that purpose-built laboratories were central to his chemical practice.[864] Trained in Bunsen's recently completed laboratory in Heidelberg, and with Kekulé in Ghent during the mid-1860s, Ladenburg made acceptance of both his professorial appointments (at Kiel in 1872, and at Breslau in 1889) conditional on the construction of new chemical institutes.[865]

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[862] On the importance of training, see Warwick 2003. Latour (1988) studied the laboratory's role in making science travel.
[863] Fischer and Beckmann 1913, 19.
[864] Fruton 1990 would be an invaluable basis for such a study.
[865] According to the *Neue Deutsche Biographie* (Vol. 13, pp. 390-391), Ladenburg also spent almost two years in Paris with Wurtz.

I have already mentioned that the integration between research, training and the laboratory also helps to explain why Hofmann and others devoted so great a portion of their working lives to the design and construction of laboratories. Chemists understood the significance of purpose-built laboratories in advertising the status of their discipline, but their laboratories were also manifestations in bricks and mortar of the integrated system of training and research by which chemical knowledge was produced. Existing institutional histories, by contrast, have tended to concentrate on the exterior of the laboratory, on its scale and aesthetics and its institutional and social setting, generally giving at best a rather hazy idea of what was going on inside. Where nineteenth-century chemists saw their laboratories in terms of content as well as context, one might say, institutional histories have focused on context whilst almost entirely ignoring content. In the following, final paragraphs of this dissertation I explore the historiographical consequences for chemistry – and for science more generally – of integrating both context and content in a history of the development of institutional chemical laboratories in late-nineteenth century Germany.

The existing historiography of institutional laboratory development is focused on the *institutional revolution* which took place in the German lands after about 1860. The applicability and usefulness of this historiography in the case of chemistry has been explicitly called into question by several institutional histories.[866] It also sits rather uncomfortably with many aspects of existing historiography derived from other approaches to the history of nineteenth-century chemistry, including its overwhelming focus on Liebig's Giessen laboratory and on the development of the chemical industry. Despite this, there has been no historically explanatory alternative account to date of the development of chemical laboratories in the nineteenth century, nor any suggestion of why the dominant historiography of *institutional revolution* could be so *right* for physics and physiology and so *wrong* for chemistry. Starting from the laboratory bench, with the daily work of chemists, this dissertation – especially this last chapter – has provided a complementary account of laboratory development from the bottom up, and I argue that this account has important consequences for our understanding of the institutionalisation of both chemistry *and* physics and physiology. Before I set out that argument, however, it will be useful to summarise how historians have perceived the shortcomings of the *institutional revolution* in relation to chemistry.

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[866] Borscheid 1976; Tuchman 1993.

When David Cahan coined the term "institutional revolution" to capture the transformation of physics brought about by the construction of palatial, purpose-built laboratories in late-nineteenth-century Prussia, he introduced a new landmark into the historiography of experimental science in academic settings.[867] Cahan's work provided a valuable corrective to the widely held view that factors largely internal to the reformed German university system, including the Humboldtian *Wissenschaft* ideal, were responsible for promoting the value of research. Nevertheless, his notion of "institutional revolution" was not without problems – especially for chemistry. It provided a useful framework for Graeme Gooday's essay on the "laboratory revolution" in British physics but, as Arleen Tuchman noted, the rise of institutional, laboratory-based training in chemistry not only began much earlier than Cahan's work suggested, it also proceeded much more gradually than his choice of the term *revolution* implied.[868] Tuchman responded to this by drawing attention to the atypical nature of the much-studied Prussian case, and she concluded from her study of laboratory science and medicine in Baden that there was no widespread *institutional revolution.* Even in the case of Prussia, Steven Turner argued that the earlier laboratories of Hermann Kolbe in Marburg and Robert Bunsen in Heidelberg had served as models for the chemical institutes built for August Hofmann at Bonn and Berlin in the 1860s.[869]

Writing more generally, Turner was concerned by the proposal of a "major discontinuity between the hesitant and small-scale attempts at the creation of institutes and the institutionalization of laboratory training which had gone on through the Vormärz period and the boom in institute-building which set in after 1860".[870] Turner's emphasis on continuity during the mid-nineteenth century was criticised by Timothy Lenoir, who argued that Turner was wrong to see Hofmann's later institutes as a "natural outgrowth" of those in Marburg and Heidelberg. Instead, Lenoir proposed that the two phases of institute building reflected a major ideological shift: early institutes existed to bring small, elite groups of students into contact with the master, while later institutes were created to impart laboratory skills to the average man.[871]

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[867] Cahan 1985.
[868] Gooday 1990; Tuchman 1993, 176. Tuchman (1993, 101-103 and 168) used the specific example of Robert Bunsen's Heidelberg laboratory.
[869] Turner 1982, 151-154.
[870] Turner 1991, 35.
[871] Lenoir 1992, 14-15.

This is not the place to examine any of these individual claims in detail. Taken collectively, however, this body of work is of significance for the present study because it shows that chemistry does not fit the dominant historiography. Cahan's *institutional revolution*, whilst helpful to historians of physics and physiology in Prussia and elsewhere, fails to convince scholars concerned with the development of chemical laboratories anywhere in Germany during the nineteenth century. Was there an *institutional revolution* in chemistry and, if so, when did it occur? How does the case of chemistry relate to physics and other sciences? What does this history of chemical practice contribute to our understanding of these questions?

This history has shown how the daily practice of chemists shaped their laboratories "from the foundations to the roof" in ways that become apparent only when we understand institutional chemical laboratories as places of work rather than exclusively as architectural manifestations of cultural or economic value.[872] Seen in this way, the development of institutional chemical laboratories certainly appears much more extended than is consistent with Cahan's *institutional revolution*. There is, however, a noticeable discontinuity around 1860 when chemists began to work in purpose-built laboratories they had themselves helped to design. This change may or may not warrant the term *revolution* but I have argued that it marked a significant break point in the institutionalisation of chemistry. These laboratories, moreover, both reflected and enabled chemists' systems of disciplined training, making them influential symbols of a new notion of what it meant to be a scientist or to practise a science, as well as powerful tools of scientific productivity.

Considering late-nineteenth century institutional chemical laboratories as badges of scientific credibility and productive utility suggests plausible new explanations for the *institutional revolution* in physics. As Simon Schaffer has shown in the case of the Cavendish laboratory, it was by no means self-evident in the 1870s that experimental physics belonged in the university.[873] Nor did physics offer the immediate industrial and commercial benefits associated with chemistry.[874] Chemists' redefinition of their discipline as a science *because* it was practised in

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[872] Wurtz 1882, 7.
[873] Schaffer (1992, 24-26) related the arguments used by James Clerk Maxwell to justify the introduction of experimental physics to the University of Cambridge.
[874] According to Schaffer (1992, 24) the main purpose of the "new British physics laboratories of 1860-1880" was to support the "imperial communications project" of international submarine telegraphy. Gooday (1990, 32-36) also noted the significance of telegraphy in the development of physical laboratories, but sought to emphasise the dual role of education in precision-measurement physics as both a cause and consequence of the "laboratory revolution" in Britain.

magnificent palaces showed that experimental science could have a place in the academic environment, and it presented a new opportunity for disciplinary development. Chemistry provided the model for new, purpose-built laboratory institutes, and it is reasonable to conjecture that physicists were eager to obtain these new scientific status symbols for themselves.[875] They were certainly able and willing to capitalise on the experience of chemists. What had taken chemists decades to achieve was emulated by physicists in a fraction of the time and – thanks to the more limited constraints placed by experimental physics on the design of the building – at substantially lower cost.[876] Institutional laboratories for the relatively new academic discipline of experimental physics rose, swiftly and apparently effortlessly, from almost nowhere. In this absolutely crucial, yet hitherto utterly ignored sense, the chemical laboratory really was what Holmes once called "the prototypical institution of the experimental sciences".[877]

Where does this leave the *institutional revolution*? Firmly in physics (and possibly physiology), I suggest, but also ripe for the enrichment a new history of the institutionalisation of chemistry would provide. Olesko had a point when she suggested that a "craft tradition seems to have been far more responsible than a scholarly one for the evolution of chemistry as a laboratory science", but we should be careful about how we interpret this claim.[878] I have shown that institutional chemical laboratories were built because they were essential to aspects of disciplinary practice. They were funded largely because of the industrial and economic benefits perceived to follow from experimental chemistry. If the institutionalisation of physics (or any other discipline) *appears* to have been driven primarily by scholarly ideals, this is because chemistry had paved the way. Its "craft tradition", far from characterising a merely empirical, mathematically unsophisticated science, not only drove the institutionalisation of chemistry but also enabled the *institutional revolution* in physics.

The *institutional revolution* in physics has appeared robust and clear-cut because historians have not looked sufficiently broadly in their quest to explain why and how so many huge physical laboratories were built within such a short time. And it has

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[875] Gooday (1990, 40) associated purpose-built laboratories with physics "newly-elevated academic status".
[876] Compare, for example, what I have said about the hazards of practical chemistry compared with those of physics. In the new University of Strasburg the chemical institute cost almost 25% more than that for physics. See Robins (1887, 65), reporting from *Nature* (1885).
[877] Holmes 1989b, 124.
[878] Olesko 1991b, 93.

come to dominate the history of late-nineteenth century science because historians have been loath to consider that what seemed historiographically accurate for physics might *not* be appropriate for chemistry. By pointing out the explanatory and descriptive inadequacies of the *institutional revolution*, this dissertation helps to undermine the position of physics as first-choice disciplinary model for historians of physical science – which ought to be good news for the history of chemistry and the history of science more generally. Chemistry, as so many of my actors have been at pains to remind us, is the ultimate experimental science. Where better to begin to take the history of practice seriously and to see what it can do for history of the sciences?

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## Appendix: Analyses of Morphine in Liebig's 1830 Notebook

| Folio | Carbon | Hydrogen | Nitrogen | Combining Weight |
|---|---|---|---|---|
| 43v (M) | *55.0%* (mass) | 6.07% | ---- | ---- |
| 44v (M) | 70.2-71.4% (mass) | ---- | **4.51%** (C) | ---- |
| 45v (M/W) | 68.5%; 69.1% (mass) | ***6.39%; 6.34%*** | **4.99%** (4.79%) (C) | ---- |
| 46v (W) | 72.0% (volume) | ---- | 4.60% (C) | ---- |
| 50v | ---- | ---- | ---- | **Sulphate salt:**<br>**9.64% water of crystallisation; 10.7% barium sulphate;**<br>(no composition given) |
| 53v | 53.9% *equiv. 69.2% C in morphine* (mass) | ---- | ---- | **Sulphate salt:***<br>**additional 4.66% "chemically bound" water;**<br>(36C, 2N, 40H, O8) and<br>(54C, 3N, 60H, O12) erased |
| 55av | Sketch of Kaliapparat | | | ---- |
| 56v | (see 63v) | ---- | *4.91%* (A) | ---- |

* Liebig (1831, 21) derived the combining weights 3659; 3554 from this data, but these calculations are not in the 1830 notebook.

| 62v | Analysis of Harnstoff | | | |
|---|---|---|---|---|
| 63v (W) | **72.3%** (mass)<br>(original data recorded at folio 56v) | **6.78%** | 4.64% (unclear) | **Chloride salt**<br>**3640; 3613**<br>**(34C, 2N, 36H, O6)** |
| 68v (W) | **72.3%** (mass)<br>*72.6% from given data* | ***6.73%*** | *2.05%* (A)<br>4.40% (unclear) | --- |
| 69v | --- | --- | **3.97%** (B) | --- |

## Notes for reading the table

(M) = morphine supplied by Merck; (W) = morphine supplied by Wittstock.

I have reported all percentage values to 3 significant figures for the sake of consistency. Liebig's calculations were not performed according to any standard method, and his handling of numerical values varied widely. His numerical working contains numerous arithmetical and rounding errors, as well as variations due to changing values for atomic weights, etc.

Figures in italics are my calculated values using Liebig's data and methods.

Entries **in bold** relate to analytical results used by Liebig in his 1831 paper.

Nitrogen was determined by one of three methods:

(A) This method combined a volumetric measurement of carbon dioxide plus nitrogen with a gravimetric determination of carbon. The equivalent volume of carbon dioxide was calculated from its mass and this was subtracted from the total volume to give the volume of

nitrogen. This application of this method to substances containing very little nitrogen gave values for nitrogen which were much too low. See Liebig (1831, 8-9).

(B) Liebig claimed this was the best available method. Nitrogen and carbon dioxide were collected together and carbon dioxide then absorbed by alkali to leave only nitrogen. See Liebig (1831, 9-11; and fig. 3).

(C) This method was similar to B, except that carbon dioxide was absorbed by ammonia. Liebig discarded this method because of the non-ideal behaviour of ammonia which introduced errors into pressure/volume corrections. See Liebig (1831, 11-12).

## Acknowledgements

I never thought I'd be here but I am.

So thank you all.*

I've had a ball.

* This piece of work was made possible by a grant from The Leverhulme Trust to my supervisor at University College, Hasok Chang. It is a pleasure to thank them both for their generous support throughout. A substantial part of my research was carried out at the Max Planck Institute for the History of Science in Berlin, where Professors Ursula Klein and Hans-Jörg Rheinberger were welcoming and generous hosts. Professor Alan Rocke helped make it possible for me to spend a fruitful and enjoyable week at the Chemical Heritage Foundation in Philadelphia, hosted by Dr Ronald Brashear and most ably supported by the staff of the Foundation's library and archive. Professor Christoph Meinel has graciously allowed me to use material from an as yet unpublished edition of the Liebig-Wöhler correspondence. Expert assistance was provided in London by the staff of the Science Museum and Imperial College Libraries, the Imperial College Archive, the Wellcome Library, the British Library, the Library and Archive of the Royal Society of Chemistry, and the D.M.S. Watson Library at University College. Equally skilled and helpful staff at the following German libraries and archives deserve a special mention for coping with my broken spoken German: the Max Planck Institute for the History of Science, Berlin; the Berlin and Munich State Libraries; the Archives of the Humboldt University and the Berlin Brandenburg Academy of Sciences in Berlin, and the Deutsches Museum in Munich. Whilst in Munich, I benefited greatly from the calm and peaceful surroundings at the Kerschensteiner Kolleg. There are many individuals whose names I could list here, but you know who you are and so do I – and I shan't forget.